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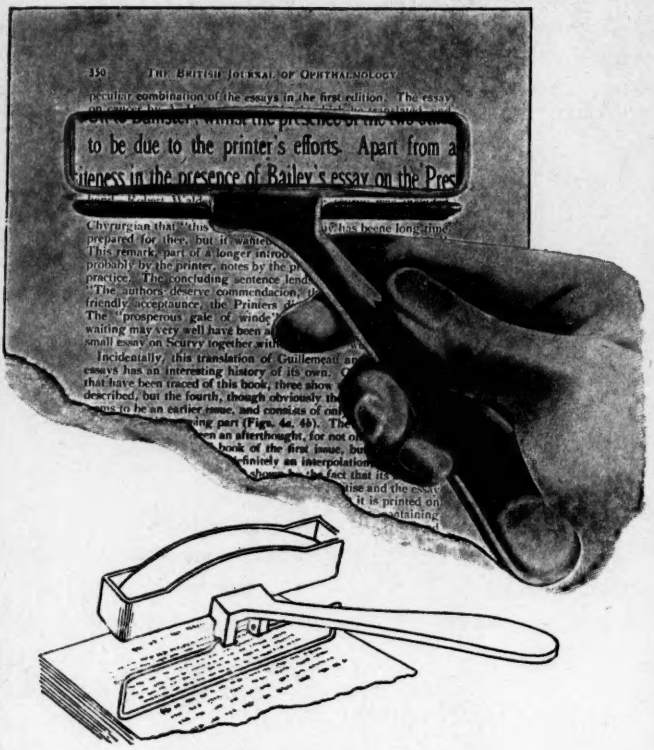

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COMMUNICATIONS

THE SCOPE OF CORNEAL GRAFTING*†

BY

B. W. RYCROFT

From the Corneo-Plastic Unit and Eye-Bank, Queen Victoria Hospital, East Grinstead, Sussex

IN considering corneal grafting it must surely be in the thoughts of all of us that we are offering our own special tribute as ophthalmologists to the pioneer work of our colleague and President, Mr. Tudor Thomas. For it was in Cardiff that he carried out that experimental and clinical work which not only inspired ophthalmic surgeons in many parts of the world to study corneal grafting, but which also went far to establish keratoplasty as an effective method of ophthalmic surgery in the treatment of corneal blindness (Tudor Thomas, 1951).

Historical Survey

The idea of corneal grafting in Great Britain may be said to have begun with the remarks of Darwin (1794-96):

> *After ulcerſ of the cornea which have been large, the inequalitieſ and opacity of the cicatrix obſcure the ſight: in this caſe could not a ſmall piece of the cornea be cut out of a kind of trephine about the ſize of a thick briſtle, or a ſmall crow-quill, and would it not heal with a tranſparent ſcar?*

This is not the earliest record of the idea of corneal grafting, but it is probably the first to have appeared in the English language. The first attempts to perform the operation were made in the first half of the 19th century; they were handicapped by constant infection, crude instruments, no anaesthesia but a bottle of brandy, no idea of selection of cases suitable for grafting, and complete confusion of thought between the biological problems of homoplasty and heteroplasty. But this new idea suggested vast potentialities; there was no scarcity of donor material and many patients were suitable for treatment as a result of indifferent methods of treating war injuries and widespread blindness from venereal infection. Many trials were made and many failures were recorded, but here and there in the literature glows the spark of a successful case (e.g., Bigger, 1837). Such cases caused Marcus (1841) to postulate that:

(1) there should be an exact correspondence in the size and form of the graft and opening;

(2) the graft must be rapidly transferred and there must be ready fixation;

(3) the internal structures of the eye must be prevented from being pushed forwards on the opening on the cornea.

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*Based on the opening paper at the Section of Ophthalmology, Annual General Meeting of the British Medical Association, Cardiff, July, 1953.

† Received for publication August 31, 1953.

Even though Dieffenbach (1830) described the idea of corneal transplantation as an "audacious fantasy", yet the important fact had been established that an animal cornea would accept other animal grafts without great disturbance, although the objective of transparency in a corneal transplant had not yet been achieved.

So unsuccessful and discouraging were the results of these early attempts that the second half of the 19th century commenced as a period of gloom. A few attempts were made to cross-graft animals, but beyond this little experimental work appears to have been carried out. Though keratoplasty did not prosper, the gloom was not quite unrelieved, for other branches of ophthalmic surgery were making progress: von Graefe (1856) demonstrated the value of iridectomy, cocaine came into use, and shortly afterwards steam sterilization, and the principles of antisepsis were being accepted. Between 1878 and 1888 von Hippel carried out experiments with corneal grafts in animals and man, and devised his clockwork corneal trephine which did so much to stimulate and facilitate graft surgery. Furthermore, he actually recorded and showed a patient at Heidelberg in 1886 and 1887 on whom he had carried out a successful animal graft which retained some degree of transparency. By the end of the century the principles of homoplasty had been soundly defined by Fuchs (1901), and the prospects for accurate corneal graft surgery, with the possibility of some improvement of vision, were bright.

The 19th century ended on an optimistic note and, though there had been many fruitless experiments, there were occasional reports of a successful case, infection was becoming less of a menace, and the idea of homoplasty was established. Better instruments were in use, and thus different techniques could be tried, so that, although there was a certain amount of confusion as to the best method, more trials of different methods were made. As yet, however, on account of the limited number of successes, there could be no adequate selection of cases.

Soon after the turn of the century Zirm succeeded in grafting the eye of a man with severe lime burns, and he followed the case for over 2 years with accurate records of improved vision. Zirm (1906) enumerated the principles on which much of modern corneal graft surgery is based:

(1) The exclusive use of young and healthy human cornea.
(2) The use of the von Hippel trephine together with eserine.
(3) Adequate anaesthesia, strict asepsis, and the avoidance of anti-sepsis.
(4) Protection of the graft between layers of gauze material and adequate retention by overlay sutures.

Recent Progress

Since that time corneal graft surgery has made rapid progress, although hindered by the two wars. Between the wars, Filatov (1934) pointed out the value of the cadaver graft, asserting that this material was as good, if not better, than fresh material, and Elschnig (1930) published a large series

of successful cases which in themselves were an inspiration. Alterations in technique came with experience: Tudor Thomas urged the bevel edge of the graft with variations in the overlay sutures, and correlated the safety of this method with careful animal experimental work. In the U.S.A. Castroviejo (1939) demonstrated a large series of successful results. More recently Franceschetti (1949) in Switzerland and Paufique and his co-workers (1948) in France have revived lamellar keratoplasty with modern technical advancements.

Thus we may now say that infection has been controlled, excellent instruments of beautiful precision are generally available, and safe anaesthesia is the rule. The selection of cases has also become more definite and the assessment of results more uniform and accurate. It is safe to say that about half the selected patients who undergo full-thickness transplantation may now expect improvement of sight with clear grafts up to 60 per cent., and that those for whom the partial thickness operation is preferred have a higher expectation of improved vision with clear grafts up to about 80 per cent.

Present-Day Problems

The difficulties which still remain may be enumerated under the headings of Technique, Administration, and Biological Problems.

(1) Technique.—As in every branch of surgery, now that principles have been firmly established there are many methods whereby successful results can be achieved. In the old days the occasional successful case created excitement, but to-day the emphasis must be placed on accurate statistical results.

(*a*) *Fixation of the Graft.*—This is still a matter of choice. Some, including our Unit, incline to the old view that the graft should be almost untouched and that fixation should depend on overlay sutures from which the graft is protected by egg membrane. We use a " Union Jack " pattern of overlay sutures giving adequate fixation around the perimeter; it is believed that this is better than the simple right-angle cross sutures which tend to cause localized distortion by uneven tension. Others feel that the graft is best secured in the bed by the insertion of separate interrupted radial sutures which hold it in place, but we consider that each stitch separates the corneal lamellae, thereby allowing oedema to develop and setting up a local area of potential vascularization. Moreover, unless these stitches are exactly at right angles to the section, a good section can be converted into a bad one as the stitches are tightened. Other surgeons have felt the need to employ splints of various materials to secure the grafts in place and obtain successful results by different techniques. Figs 1 (*a*, *b*), 2 (*a*, *b*), 3, and 4 (overleaf) show examples of modern corneal graft surgery by different methods.

(*b*) *Cutting the Graft.*—This is an important consideration because an accurate section line is of great importance if rapid reformation of the anterior chamber is to be achieved and iris inclusion avoided. Individual surgeons again have different methods. In our view the edge of the graft should be traumatized as little as possible and we prefer to cut it by the punch method which compresses

FIG. 1 (*a*).—"Primrose" keratitis.—Diffuse corneal scar not extending to Descemet's membrane.

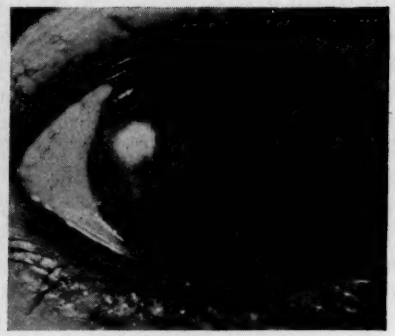

FIG. 1 (*b*).—8-mm. lamellar graft, vision 6/9. Note image of white-coated photographer and iris pattern.

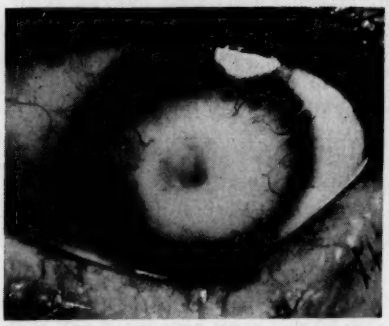

FIG. 2 (*a*).—Old traumatic burn keratitis.—Before operation, previous corneal graft in 1934.

FIG. 2 (*b*).—Full thickness 6/8-mm. flange graft, vision 6/12. Re-graft.

FIG. 3.—Flange graft.—Centre circle 6 mm. and full thickness; corneal lamellar frill for sutures 2 mm.

the fibres at the edge of the graft. If the graft is cut by a trephine which is not exquisitely sharp these fibres are separated. Since excellent

FIG. 4.—Interstitial keratitis.—Full-thickness 6-mm. cylinder graft one month after operation, fixation by author's technique, vision 6/36 (Senile cataract). Re-graft.

results are now obtained by various methods, details of technique no longer form a major problem.

(*c*) *Selection of Cases.*—Where the scar can be seen by the narrow slit-lamp beam to invade the corneal stroma to the level of Descemet's membrane, a penetration graft is the method of choice. Lamellar keratoplasty is more suitable for cases in which a clear area of cornea can be seen to overlay Descemet's membrane. Mustard gas cases have always presented difficulties when an initial full-thickness graft is used, owing to the sharp irregularities which occur in a mustard gas cornea. At one point the thickness may be little more than Descemet's membrane, whereas at another point in the same cornea there may be an actual increase in thickness. Ocular pemphigus where the cornea is dry has given uniformly unsuccessful results in eight cases at our Clinic, and it is also felt that where a symblepharon does not invade corneal tissue it should be left alone if an optical graft is contemplated on that cornea. Keratitis acne rosacea has occasionally been found to invade successful grafts some months after operation, but this should not prevent treatment of such cases by keratoplasty; repetition grafts have been strikingly successful in acne keratitis, corneal dystrophies, and interstitial keratitis. Even with modern improvements in the operation, it is felt that a penetration graft is only justified where binocular vision is no better than a poor 6/36. A unilateral penetration graft where the other eye has good vision is rarely indicated.

(2) Administration.—The supply and preservation of donor material is another major problem, but one which is diminishing in gravity.

(*a*) *Supply of Donor Material.*—Before 1939 the supply of donor material from eyes which had had to be excised was adequate for the limited number of corneal transplantations which were then undertaken, but since 1945 the stimulus provided by the work of Castroviejo, Franceschetti, Paufique, and others has caused the demand for donor corneae to outstrip the supply. Filatov had shown that cadaver material was just as good as fresh, but as the law stood in Great Britain, it was not possible to obtain such supplies legally. Yet if corneal graft surgery was to advance an adequate donor supply was necessary for trials, treatment, and training. It was therefore decided to try either to amend the existing Anatomy Act of 1832 or to bring in a new Act of Parliament. By careful factual propaganda the people were shown by the press, radio, and television what corneal graft surgery could be expected to do for blindness, and when the Corneal Grafting Act came before Parliament it was passed without opposition in September, 1952. This Act, which permits eyes to be removed from a corpse where no objection has previously been made by deceased or relatives, or where the eyes have been bequeathed, promises to solve the donor problem (Rycroft, 1953).

(*b*) *Selection and Preservation of Donor Material.*—The best eyes come from aged persons who have died a natural death. They should be removed within 10 hours of death, and after removal may be kept under conditions of sterile refrigeration for at least a fortnight. It is most essential that a culture of donor eyes should be taken immediately on receipt at the Eye Bank and again 48 hours before use; in about 10 per cent. of cadaver eyes after several days' refrigeration at 4° C. pathological organisms have been cultured. At the East Grinstead Unit the eyes are received in liquid paraffin and an immediate culture is taken. They are then transferred to the Eye Bank in a mixture of liquid paraffin, streptomycin, and peni-

cillin. The container holding this medium and the eye is then placed in the refrigerator at 4° C. until required for use when a further culture is taken. Eyes have given successful optical grafts after preservation by this method for as long as 3 weeks.

(*c*) *Training of Personnel.*—This has become a problem for the future now that adequate donor material is available. In our view this type of surgery should only be undertaken in selected centres. To carry out corneal grafts at random intervals at hospitals of all types is not only extravagant in the provision of expensive instruments and wasteful in donor material, but also exposes the patient to risks of inadequate technique and donor supply. At least three donor corneae should be at hand before any graft case is undertaken. The operation is one of great precision demanding much practice in technique and a long clinical training in the selection of cases. If anyone is to practise it with consistent success he must work under conditions where the patient has adequate safeguards. Then again, the arrangements for the collection and banking of donor material are better carried out in special centres than in miscellaneous hospitals: donor material is still too valuable to waste.

(3) Biological Problems.

(*a*) *Antibody-Antigen Reaction.*—This problem, which confronts all branches of reconstructive graft surgery, depends broadly on the reactions of the host to grafts of foreign tissue. Under normal conditions the body will not accept a true graft of another person's tissue, except in the case of uni-ovular twins. A homoplastic skin graft from another person invariably disintegrates at the end of about 3–4 weeks, but the cornea and certain pieces of cartilage are favoured materials and behave differently, since a corneal graft is not cast off and cartilage apparently remains unchanged. The present view is that such a corneal graft loses its cellular characteristics at the end of a fortnight but retains basic membranes. Invasion of these membranes by cells from the host, of which there are not many, reconstitute the graft: thus this is not a true graft but a scaffold graft which becomes integrated with the membranes and cell contents of the host. It is also considered that the presence of cells in the corneal graft stroma is essential for transparency. Loss of transparency constitutes failure of the graft; vascularization and oedema are the main dangers.

(*b*) *Vascularization.*—This may occur in the first week, when it is irritative, superficial, and due to operative trauma: this is of little consequence and generally subsides. Deep vascularization, however, is another matter; it may be caused by premature operation when the initial disease has hardly subsided; it may also be caused by defects of technique, broad iris adhesions, or the infiltration of existing vessels. There still remain, however, a considerable number of cases in which the graft fails from vascularization when the technique has been entirely successful, and it is possible that this group of failures is due to the antigen-antibody reaction. Local cortisone is definitely helpful in neo-corneal vascularization but it has little effect on established vessel systems.

(*c*) *Oedema.*—This is also a menace, and though it is frequently associated with vascularization there are cases in which blood vessels are not unduly prominent. Again, deficiencies of technique which do not allow an accurate edge-to-edge alignment of the graft and host frequently account for oedema, but often after

successful technique there may be a severe and persistent oedema with bullous formations in the graft epithelium which begins about the third week without any sign of undue irritation and which causes a failure of the graft: in such cases tissue allergy is probably the cause also (Fig. 5*a* and *b*). The solution of these problems is our responsibility for the future, but already there are signs of encouragement.

Billingham and Medawar (1950) in London and Maumenee and Kornblueth (1948) in San Francisco have proved beyond doubt that the insertion of a skin or corneal graft into the host will produce an antigen-antibody reaction and that there is some definite relationship between the two. This biological problem and confirmation of the work of Maumenee is at present being studied in our Unit and in the laboratory.

FIG. 5 (*a*).—Graft oedema 8 weeks after operation.

FIG 5 (*b*).—12 weeks after operation. Graft 6·1 mm. and interrupted suture fixation. Note absence of host vascularization and oedema of suture tracks.

But the initial failure of a graft from the antigen-antibody reaction does not necessarily constitute a permanent failure. Grafts have been repeated in several cases after one or two failures with a final successful clear graft (Fig. 6*a* and *b*). At each attempt the technique was identical but in the failures oedema or vascularization intervened whereas the final graft produced no reaction and remained clear.

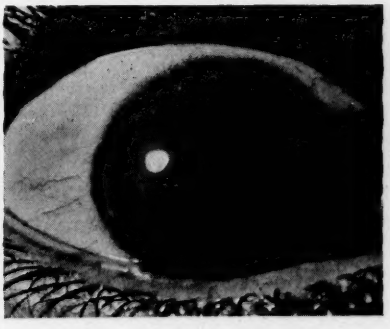

FIG. 6 (*a*).—Corneal dystrophy before operation.

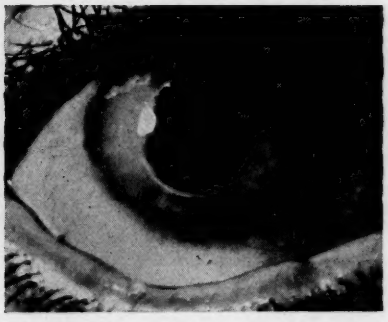

FIG. 6 (*b*).—Full-thickness 6-mm. cylinder graft 6 months after operation, fixation by author's technique, vision 6/9, re-graft.

FIG. 7 (*a*).—Total corneo-scleral transplantation.—Eye before operation, large leucoma adherens.

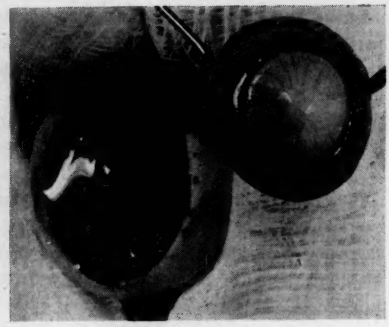

FIG. 7 (*b*).—Graft cut from cadaver eye.

FIG. 7 (*c*).—Scarred cornea and scleral frill excised under low-pressure anaesthesia: the intra-ocular pressure was very low and there was no bleeding.

FIG. 7 (*d*).—Graft sutured in position.

FIG. 7 (*e*).—Grafted eye 3 weeks later; at 6 weeks the cornea was totally opaque but there was no infection.

Section of the enucleated eye showed good union of the incision and diffuse corneal oedema.

The investigation and solution of these reactions of tissue transplantation are of paramount importance for all branches of reconstructive surgery, for this is likely to be the era of surgical transplantation in several parts of the body. The eye, because of its ready accessibility and individual reaction, will prove most useful in future studies.

Future developments may include grafts of the whole of the cornea with some part of the sclerotic also. Technically it is now possible to graft the whole of the cornea and part of the sclera in one piece without undue difficulty, but it is not yet possible to maintain such a grafted cornea

in permanent transparency. Always at the end of three weeks, in a very similar manner to a skin graft, the cornea has become opaque and fibrosed, not from infection but from innate biological causes. When a whole graft of this kind remains clear it will represent a major step in the treatment of corneal blindness (Figs 7*a–e*).

The words of de Wecker (1897) are as true to-day as they were when written:

> We have no right in these cases to refuse the slightest aid to sufferers who have but this one remaining chance to recover a little sight: neither should we be deterred by the reproach of eccentricity which will certainly be levelled at anyone who therefore attempts to graft a cornea.

I wish to thank Mr. Giles Romanes and my staff for their constant help, Mr. Gordon Clemetson and the staff of the Photographic Unit for their assistance and expert photography, and Mr. LeFanu, librarian of the Royal College of Surgeons of England, for his assistance. It is a pleasure also to acknowledge the assistance this Unit has received from many ophthalmic surgeons and pathologists in the South of England with the supply of donor eyes.

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OPACIFICATION IN PERFORATING CORNEAL GRAFTS*†

BY

A. G. LEIGH

From the Institute of Ophthalmology, London

As the success of a grafting operation ultimately depends upon the transparency of the graft, the problem of opacification is of great interest and practical importance to the ophthalmic surgeon. This paper is the result of the study of some fifty personal cases in an attempt to elucidate certain aspects of the problem as it occurs in perforating corneal grafts.

A graft may become opaque for one of three reasons:

(1) Incorrect choice of case.

(2) Faulty operative technique or inadequate post-operative treatment.

(3) Late complication in a graft which, during the immediate post-operative period, appeared to be progressing satisfactorily.

Pre-operative Condition of Recipient Cornea and Fate of Graft

Opacities

Isolated Central Opacity.—The ideal case for a perforating corneal graft is represented by a central, non-vascularized corneal nebula which can be removed completely by trephining. Fig. 1 shows the result in such a case. Here the whole nebula was included in the excised disc and the graft was laid in clear, normal cornea. Optical section shows that the only points of opacification at the junction of host and graft are at Bowman's and Descemet's membranes, the union through the substantia propria being clear and almost indiscernible.

Completely Opaque Cornea.—The worst type, of hopeless prognosis for the simple perforating graft, is the complete opacity involving the whole area and thickness of the cornea. This may be associated with gross changes in structure so that the cornea is replaced by abnormal tissue frequently the seat of degenerative changes. A penetrating graft placed in a cornea of this nature rapidly becomes opaque.

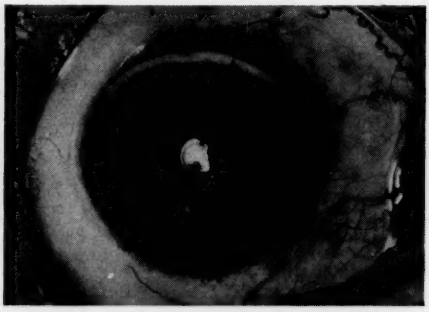

Fig. 1.—Perforating corneal graft for central nebula.

Intermediate Types.—If discrete islands of opacity occur in what

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†Paper read to the Section of Ophthalmology at the 121st Annual Meeting of the B.M.A., Cardiff, July 1953.

appears to be otherwise structurally normal cornea the prognosis is good, even though the combined effects of multiple lesions of this type may result in considerable opacification, This type is seen in the more severe varieties of interstitial keratitis; Fig. 2 is an example of a diffuse opacity involving both corneae, the visual acuity in each eye being reduced to counting fingers at 2 ft. The grafts have remained clear for 2½ years in the left eye and for one year in the right eye with visual acuity 6/6 and 6/9 respectively.

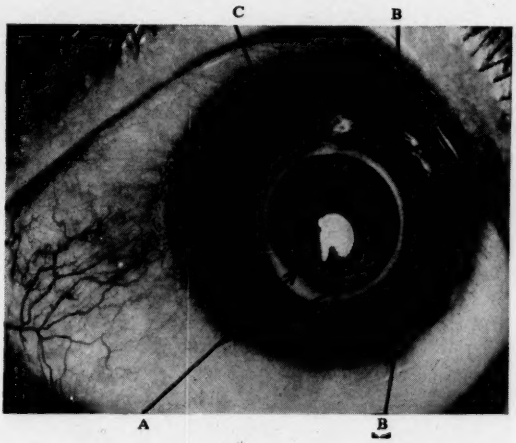

FIG. 2.—Perforating corneal graft of 2½ years standing in case of old interstitial keratitis.

A. Marginal opacification of graft adjacent to area of densest opacity in recipient cornea.

B. Persistent deep vascularization not entering graft but forming loops at host/graft junction.

C. Organized exudate in pupil.

Incomplete opacities associated with fibrosis, or hyaline or other degenerative process, are more likely to produce opacification within the graft particularly if these areas are in direct contact with it. Fig. 3 shows such an area of fibrosis within the recipient cornea and its effect upon the adjacent graft.

FIG. 3.—Perforating graft for diffuse opacification of stroma and associated vascularized superficial nebula.

A. Opacity in margin of graft adjacent to dense corneal opacity.

B. Vessel which supplied superficial opacity persists but does not involve graft, extending only to margin of graft.

In another case a leucoma adherens was trephined out, the iris abscissed, and a graft immediately placed in position. A very small portion of the opacity remains throughout the thickness of the cornea, but this appears to have been sufficient to stimulate the formation of a similar opacity in the adjoining graft, the remainder of which is clear.

Similarly (Fig. 4) a brush-like opacity developed in the stroma of a graft at the point of contact with the denser (presumably fibrotic) area of the residual opacity.

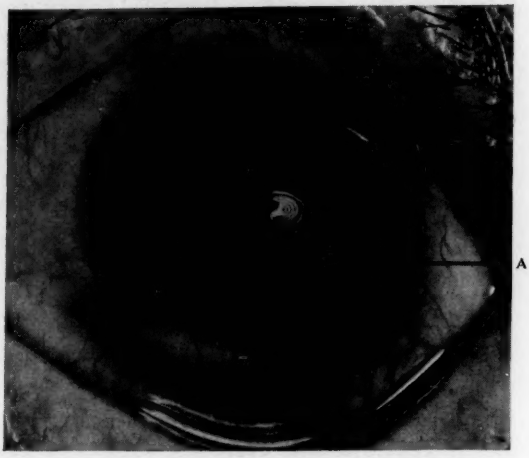

FIG. 4.—Brush-like opacity (a) extends into stroma of perforating graft, apparently originating from an area of similar opacity in recipient cornea.

The fate of a graft depends largely upon the condition of the cornea into which it is placed. A clear recipient cornea will maintain a clear graft, a completely opaque cornea will beget an opaque graft. We are faced therefore with the problem of deciding how much opacification will render a cornea unsuitable for a simple perforating graft. I suggest the following criteria:

Good results may be expected with:

(*a*) A central localized corneal nebula.

(*b*) A diffuse opacity occurring in a cornea in which the separate elements of the structure are still distinguishable.

(*c*) Dense opacities of Descemet's membrane, provided that the remainder of the cornea is relatively clear.

(*d*) The presence of one-third or more of clear cornea of normal structure.

Poor results may be expected with:

(*a*) A completely opaque cornea.

(*b*) The presence of fibrosis, hyaline or other forms of degeneration unless these occur only in scattered islets.

(*c*) Gross superficial opacification especially if associated with degenerative changes.

Vascularization

Superficial Vascularization.—This presents a serious problem for it frequently occurs in association with gross changes in the corneal epithelium and the subjacent tissue. This type of vascularization is of two main varieties:

(*i*) one or two large vessels passing to the site of some old superficial lesion;
(*ii*) many fine vessels invading the cornea from all points of the circumference and frequently associated with generalized opacification and patches of degeneration.

The presence of one or two large vessels does not constitute a contra-indication to a perforating graft, provided that the nature of the opacity (as discussed above) is otherwise favourable and that a considerable amount of the opacity supplied by the vessel can be included in the trephine disc. In most of these cases this vessel will not invade the graft (Fig. 3) but will extend to the line of union, where it will form a loop and then return to the limbus. Multiple fine superficial vessels are likely to cause trouble and invade the newly inserted graft. This complication is due to the presence of a type of opacity associated with fine superficial vascularization rather than to the invasive propensity of the fine vessels, the vascularization following, rather than causing, the opacification.

Deep Vascularization.—Although there is an intimate relationship between the presence of opacities and the vascularization of a graft, my experience suggests that the role of deep vascularization in the causation of opacification in grafts has been over-emphasized. On several occasions I have performed a perforating keratoplasty on an eye, the seat of old interstitial keratitis, where there has been considerable deep vascularization. Within a few days of the operation an acute reaction has occurred with the development of an extensive salmon-patch in the recipient cornea. With the exception of a few very fine deep vessels appearing within the graft on about the tenth day and disappearing some 3 to 4 weeks later, the grafts appear to be completely unaffected by the gross vascularization of the adjacent cornea, and in none of them has opacification occurred. In certain corneae some of the deep vessels of the salmon-patch persist (Fig. 2); these do not, however, enter the graft but form loops at the host/graft junction.

Immediate Post-Operative Complications

Dislocated Graft.—If, at the first dressing, a graft is found to be so grossly displaced as to require further suturing, then opacification is almost certain to occur. Such a graft is opaque when first seen, presumably as a result of the inbibition of fluid from the conjunctival sac. Even if the graft is successfully sutured into position clearing does not take place. Possibly this is due to the cut edges of both the trephine hole and the graft being sealed off with exudate so that the transference of tissue fluid between the host and the graft is prevented and the graft remains opaque. A graft which is slightly tilted, so that a small portion of the edge is elevated above the level of the recipient

cornea, does not become opaque, even in the vicinity of the ectasia. This is probably due to the rapid epithelialization of the exposed surface.

Loss of Vitreous.—The loss of vitreous, which may occur during an attempt to graft an aphakic eye, results in the development of an opaque graft. A possible explanation for this is that the interposition of vitreous between the graft and the recipient cornea prevents the exchange of fluid between them.

Infection.—Severe conjunctivitis, especially if seen at the first dressing, is a most serious complication, for it leads rapidly to opacification of the graft. It is interesting to observe that a small hypopyon, caused by the infection of a too deeply placed suture in the recipient cornea did not cause an opacity of the graft; but in this case there was no significant degree of conjunctivitis.

Anterior Synechiae.—These may be observed at the first dressing, and are frequently associated with slight clouding of the graft, which may in some cases progress to complete opacification. Anterior synechiae are a serious complication of corneal grafting, and, except in complicated cases such as leucoma adherens, occur as a result of faulty operative technique.

Oedema of the Graft.—This has occurred (*a*) in association with an infection; (*b*) concurrently with opacification due to the graft having been laid in a completely opaque cornea; (*c*) in two cases where the origin of the opacification was obscure.

In these last two cases a localized superficial oedema appeared in the graft during the immediate post-operative period. This condition persisted in one graft for 3 months and in the other for 6 months; after it had dispersed the grafts were quite clear.

I have not seen in my series the classical "*maladie de greffon*".

Late Opacification in a Clear, or Relatively Clear, Cornea

Apart from opacities which occur as the result of an unsuitable choice of recipient cornea or following a well-recognized complication, there remain those which develop suddenly in a graft which has seemed to be progressing favourably.

Case 1.—A female aged 58 had bilateral interstitial keratitis involving the central areas of the corneae, a most suitable type of eye on which to perform a keratoplasty. After a 5-mm. perforating graft the post-operative period was without incident, the graft being well-placed and clear except for a slight haze in the posterior layers; this haze was so fine as to cause no concern, being very similar to the post-operative haze which is sometimes seen and which clears leaving a transparent graft. This condition persisted for over 2 months with no apparent change when, quite suddenly, in the 14 days which elapsed between one visit and the next, the graft became completely opaque. It is necessary to emphasize that the opacity was not localized to the posterior portion of the graft but that the whole thickness of the graft was opaque. A further perforating graft of slightly larger diameter was performed and the opaque disc of the previous graft completely removed. Microscopical examination (Fig 5, opposite) showed a thick band of fibrous tissue spreading over the posterior surface of the cornea and obliterating the endothelium.

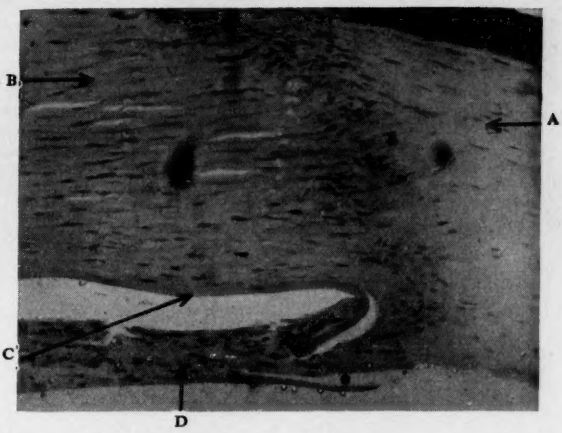

FIG. 5. — Section through graft/host junction of a completely opaque graft.

A. Recipient cornea.

B. Opaque graft.

C. Descemet's membrane.

D. Fibrous tissue extending over whole of posterior surface of graft.

Case 2.—This was due to an infection when a diffuse opacity appeared as a result of a severe post-operative conjunctivitis. This opacity was dense though not complete, but quite suddenly, again between visits, the graft (Fig. 6) became opaque throughout its whole thickness. This eye also was successfully regrafted (Fig. 7).

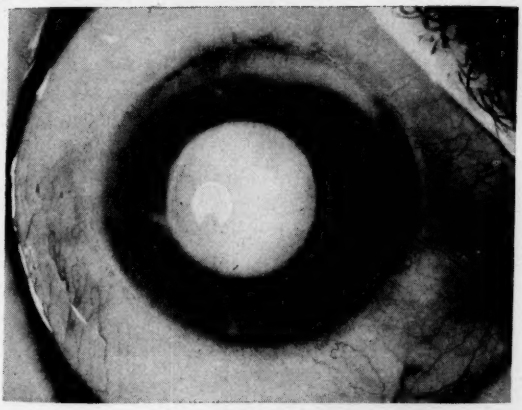

FIG. 6.—Post-operative opacification of perforating graft.

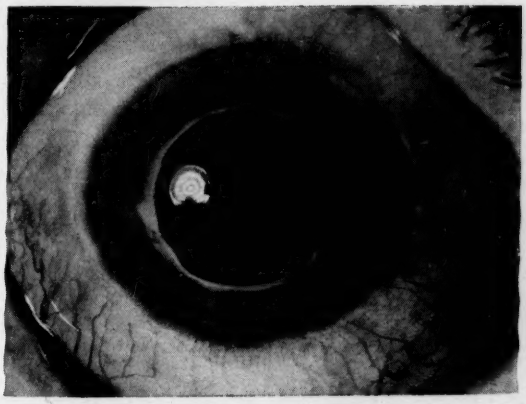

FIG. 7.—Case shown in Fig. 6 after re-grafting. This graft has remained quite clear since the operation 7 months ago.

Microscopical examination of the disc (Fig 8) showed a thick band of fibrous tissue growing over the posterior surface of Descemet's membrane, obliterating the endothelium, and presenting a picture remarkably similar to that seen in the first case.

FIG. 8.—Section of opaque graft shown in Fig. 6.

A. Opaque graft.
B. Descemet's membrane.
C. Fibrous tissue extending over posterior surface of graft.

It is reasonable to suppose that the sudden complete opacification in these two cases resulted from the cutting off of the endothelium from the anterior chamber, thus disturbing the normal fluid interchange between the graft and the aqueous so that oedema developed. As this oedema was unrelieved, hyaline changes followed and a permanent opacity was formed in the corneal stroma.

METHODS OF DEALING WITH THESE PROBLEMS

Choice of Case.—The full cooperation of the patient is absolutely essential for the success of a grafting operation; for, however effective may be the fixation of the graft, it will be incapable of withstanding much disturbance during the first few days. It is essential, therefore, that the post-operative demeanour of the patient be correctly assessed. Young children should never be submitted to a perforating graft as they are quite un-cooperative, and I am inclined to the view that this operation should not be performed on any child under the age of 15 years. The psychological disturbance in certain patients is considerable and this may result in the patient losing all control of his actions and rubbing and squeezing his eye so that the graft is displaced, or, even in less severe cases, the lack of cooperation is such that the essential daily post-operative treatment cannot be carried out.

Operative Technique.—Whilst it is beyond the scope of this paper to describe my method of grafting, there are certain points of technique which I regard as extremely important in the prevention of post-operative opacities.

(1) The graft I cut by punching out. This method has two advantages:

(*i*) The graft is perfectly cut and there is no likelihood of rough, irregular edges,

especially at the level of Descemet's membrane, which can occur when the graft is trephined from the donor cornea.

(ii) The lamellae of the graft are kept compact by punching, whereas trephining tends to separate them. I consider that the compact lamellae play a most *important part in the prevention* of the invasion of vessels from the recipient cornea.

(2) The recipient cornea is cut by the same trephine with which the graft was cut. This enables a bung-like fit to be obtained between the graft and the host, so that, even before the patient has left the table, the anterior chamber has commenced to reform and the cornea is clearly seen to be separated from the iris. This prevents the development of anterior synechiae to the graft, and of peripheral anterior synechiae which may assist the development of post-operative glaucoma.

(3) I do not use direct sutures through the graft because this subjects it to considerable trauma by grasping and by the passage of the sutures, thereby opening up the lamellae and rendering oedema, vascularization, and opacification more likely. Again, however well the sutures are placed, some distortion of the fit of the graft in the recipient cornea must occur, so that there is more likelihood of a leakage of aqueous. For fixation I use two mattress sutures placed at right angles; the main technical point being that the sutures cross the graft and enter the recipient cornea as close to the margin of the graft as possible, so that there is very little lateral movement of the suture, which remains in correct position over the graft.

In my series I have experienced only two cases of post-operative anterior synechiae: one occurred on the occasion of a second attempt at a perforating graft, and the second where, after the removal of a leucoma adherens, a thin strand of iris remained attached to the cornea. No case of the series has developed post-operative glaucoma. The adhesion of the pupillary margin of the iris to the graft, or the formation of peripheral anterior synechiae (which may be the cause of post-operative glaucoma), are prevented by the rapid re-formation of the anterior chamber.

Post-Operative Treatment.—The first dressing of the graft should be done between 36 and 48 hours after the operation—never later. At this dressing a culture is taken of the conjunctival sac and 1 per cent. atropine drops together with gutt. penicillin are instilled; subsequently antibiotic drops are instilled twice daily and atropine once daily. Once every day the eye is cocainized and the cornea carefully cleaned of all mucus that may be adhering to it. Cortisone drops are begun on the 10th day and continued for several weeks. The sutures are removed between the 10th and 14th days; sutures left in for 14 days or more sometimes produce slight superficial opacities of the graft which usually disappear in a month or so. Such opacities do not interfere with vision as my sutures do not cross the centre of the graft.

Summary

Opacification in corneal grafts is usually due to incorrect choice of case, faulty operative technique, or inadequate post-operative care.

Two cases are described in which an opacity occurring after 6 to 8 weeks

was found to be due to the development of a plaque of fibrous tissue over the posterior surface of the cornea.

Certain points of operative technique are discussed; the importance of a compact graft, the value of indirect as opposed to direct sutures, and the necessity for the immediate re-formation of the anterior chamber are stressed.

I am indebted to Dr. C. H. Greer of the Department of Pathology, Institute of Ophthalmology, for the pathological reports, and to Dr. Peter Hansell and his staff in the Department of Medical Illustration, Institute of Ophthalmology, for the photographs.

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SLOPE OF SIDES OF CORNEAL GRAFTS AND RECIPIENT BEDS*

BY

I. C. MICHAELSON

Haifa, Israel

IF a corneal graft is not properly coapted to its bed, a series of complications may ensue. These have been summarized by Barraquer (1950). A cause of this lack of coaptation is that the sides of the graft or of the bed may not be vertical, and that if sloping they may not slope in similar directions. A series of simple tests were therefore carried out to determine:

(*a*) The direction of the sides of the graft and how to influence it by the method of cutting the graft.

(*b*) The direction of the sides of the bed and how to influence it by the method of preparing the bed.

Material

Thirty-four human cadaver eyes were used. In each case the graft or bed was examined with the loupe and the dissecting microscope. Examination by means of the loupe is facilitated if the graft is placed on a blackened glass slide.

Cutting the Graft (Fig. 1)

(1) In thirteen eyes, 5-mm. grafts were cut with the cornea in position. The eye was held between the fingers, which exerted a *firm but gentle* pressure on the sides of the globe.

In nine cases the sides of the graft showed a slight convergence from the epithelial to the endothelial surfaces.
In three cases the sides of the graft were oblique and parallel.
In one case the sides of the graft were vertical.

(2) The same experiment was repeated with three other eyes, *no pressure* being exerted by the holding fingers on the sides of the globe.

In all three cases the sides of the graft showed a marked convergence from the epithelial to the endothelial surfaces.

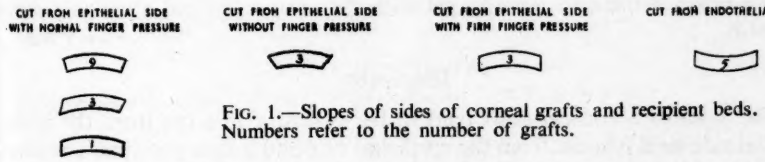

FIG. 1.—Slopes of sides of corneal grafts and recipient beds. Numbers refer to the number of grafts.

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(3) The same experiment was repeated with three more eyes, a *very firm* pressure being exerted by the holding fingers on the sides of the globe.

In all three cases the sides of the graft were vertical.

In cases in which the intra-ocular pressure is not increased by the holding fingers, the cornea is dimpled by the trephine during cutting; in those cases where the intra-ocular pressure is increased by the holding fingers the cornea is not dimpled. It would appear, if the pressure of the trephine can produce a marked concavity of the corneal surface, that the graft edges converge inwards, the amount of the convergence being proportional to the concavity of the cornea.

(4) In five eyes the cornea was first removed and cut from the endothelial surface.

In all cases the sides of the graft were vertical.

The following conclusions may be drawn from these experiments:

(*a*) If the cut is made from the epithelial side of the cornea, the sides tend to be convergent.

(*b*) Pressure on the globe during cutting of the graft tends to make the sides vertical.

(*c*) If the cut is made from the epithelial side of the cornea, a definite proportion of grafts show parallel sloping sides.

(*d*) If the cut is made from the endothelial side of the cornea, the sides tend to be vertical.

It should be emphasized that the nature of the slope of the graft as described above, can be determined in an operating theatre if a loupe is used and the graft is placed on a black glass slide.

Preparing the Bed

This experiment was carried out on ten eyes. The bed was prepared with the same care as used in the operating theatre. That is, the trephine incision was completed if necessary with scissors as soon as it became clear that the anterior chamber had been entered.

In three eyes it was practically unnecessary to use scissors. In each case the sides of the bed converged from the epithelial to the endothelial surface.

In seven eyes it was necessary to complete a good portion of the circumference of the bed with scissors.

In each case the side of the bed cut with the trephine showed a slope inwards (Fig. 2*a* and *b*). The side cut with the scissors showed in its first portion a variable length sloping outwards and parallel to the side cut with the trephine. The portion of this side actually cut with the scissors showed a variable slope inwards.

Discussion

The sides of a corneal graft tend to be vertical if it is cut from the endothelial side or if it is cut from the epithelial side and a firm pressure is exerted by the holding fingers. Otherwise the sides tend to be convergent from the

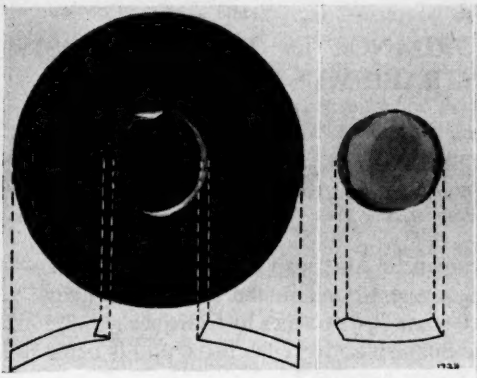

FIG. 2*a*.—Slopes of sides of recipient bed, and shape of disc removed.

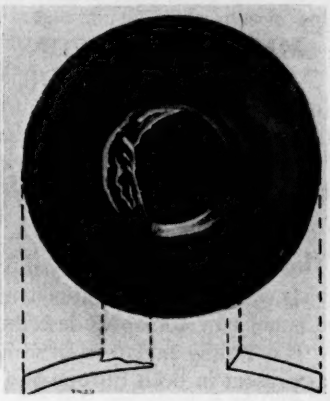

FIG. 2*b*.—Slopes of sides of recipient bed.

epithelial to the endothelial surfaces. In a definite proportion of cases, however, the sides of the graft are oblique and parallel. Such facts may have a clinical application in the operating theatre, and these possibilities are at present being investigated. For example, in one case where the sides of both graft and bed were oblique and parallel, the graft was orientated to conform to the slopes of the sides of the bed.

Summary

(1) The slope of the sides of a corneal graft cut with a trephine is shown to be vertical, convergent, or obliquely parallel.

(2) The factors influencing the direction of the slope are indicated. These include cutting from the epithelial surface, cutting from the endothelial surface, and intra-ocular pressure.

(3) The sides of the recipient bed are either convergent from the epithelial to the endothelial surfaces, or show parallel sloping surfaces modified by the projection of deep propria and endothelium which may result from the use of scissors.

(4) In cases where the sides of both the bed and the graft are sloping and parallel, the latter may be manoeuvred to conform with the sides of the bed.

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METHOD OF CONCORDANCE IN THE DIAGNOSIS OF STRABISMUS*†

BY

JOSEPH I. PASCAL

From the Department of Ophthalmology, N.Y. Polyclinic Medical School and Hospital, New York

THIS method is practically unknown to American and British ophthalmologists, and is not mentioned in any text-book in the English language, yet it is not new, for it was described some 30 years ago by Marquez (1942, 1952).

It is briefly explained in some Spanish and French texts, and is being used at present in both Europe and South America.

The most probable reason why the method has not been described in the English text-books is that it had to be used with a muscle schema which was not easy to remember, to visualize, or to apply. But the method lends itself admirably to the Benzene Ring Muscle Schema as will be shown presently. As to its value, one need not subscribe to the view (Rivas Cherif, 1949) that it is the *best* method for diagnosing paralytic and spastic strabismus, for it has good and bad points like all other methods. But it should certainly be known and used, on occasion at least, by every ophthalmologist.

The answer to the question whether we need one more method of diagnosing strabismus is best given in the following quotation from Scobee (1952):

> I recently had the rather dubious pleasure of seeing a patient with a vertical imbalance who had previously consulted seven quite reputable ophthalmologists. The patient had carefully tabulated the diagnoses and recommendations of all seven. Truth is often stranger than fiction. Of the eight vertically acting muscles, all but the left inferior oblique had been solemnly identified as the offending muscle. The patient was a person of average intelligence and could hardly be blamed for his somewhat cynical attitude. His problem, obviously enough, was how to know whom to believe, and by the time I saw him he was loth to believe anyone. Cases such as the one mentioned are not isolated instances, unfortunately, but are almost everyday occurrences . . .

In view of the above statement, another method of diagnosing strabismus may be worth knowing.

Method and Apparatus

No extensive or expensive equipment is required. The only apparatus is a pair of goggles with one red and one green filter (to know which image belongs to which eye), a small, round light (5 or 10 mm.) to serve as target for the first four steps of the examination, and a linear light " target " (12 to 15 cm. long), preferably in the form of an arrow, for the last step in the examination.

The method is essentially a co-ordination of five diplopia tests, the findings of which are grouped on a muscle schema. The letters P and S, and a dot (·) are used

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to denote paralysis, spasm, and " neutral " or indeterminate. The muscle which has the greatest agreement or concordance with the same letter is the affected muscle, as will be readily understood from the illustrations.

The Five Diplopia Tests.—These can be made for any distance of fixation, but usually 6 or 7 ft. from the patient. The red and green filters are placed before the patient's eyes, over his correcting lenses if necessary, red before the right eye (red-right) and green before the left eye. The five tests are always best made in the following order:

(1) Round light directly in front of patient's fixing eye in primary position, to determine which image is higher and which is lower.

(2) With the patient's head held steady, the target is moved to four diagnostic corners (up and left, down and left, up and right, down and right) to determine in what part of the field there is the greatest vertical separation of the images. Right and left refer to the patient's right or left eye throughout.

(3) With the target directly in front of the patient, his head is tilted towards the right and left shoulders to determine where the *vertical* separation of the images increases.

(4) With the target on the side opposite to that where the greatest vertical separation was found in Test 2, the horizontal relation of the two images is determined (crossed or uncrossed diplopia).

(5) Using the vertical line of light which is also placed on the side opposite to where Test No. 2 showed the greatest vertical separation of the images, we determine which image is tilted and how.

Pascal Muscle Schema.—To understand and apply this method easily one must know the Benzene Ring Muscle Schema (Fig. 1)*, in which each of the six extra-ocular muscles is placed on one of the six limbs of the ring, each muscle as its name connotes. The *complete* action of each muscle is shown by the position of the limb (supraduction–infraduction), by the position of the middle dot on the upper and lower limbs (adduction-abduction), and by the slant of the limb (intorsion–extorsion). The direction of the greatest up or down action of the vertical muscles is indicated by the position of the upper and lower limbs, which may be considered as " windows " facing in a certain direction.

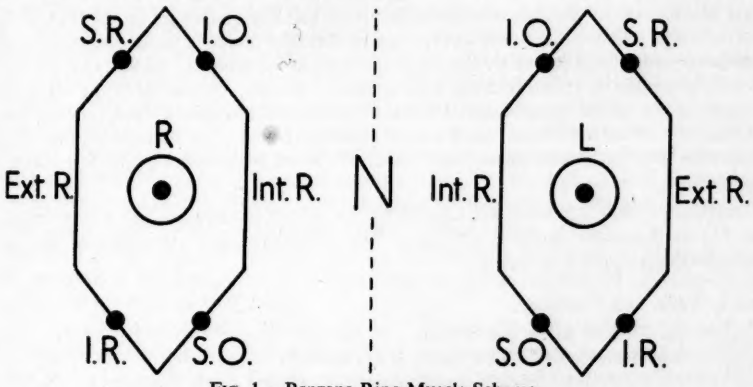

FIG. 1.—Benzene Ring Muscle Schema.

* A full discussion of this schema with its sixteen applications is given in Pascal (1952).

Application

Case 1, Tests and Findings.

(1) Red light lower, green light higher.
(2) Vertical separation of images greatest down and left.
(3) Vertical separation of images increases on tilting head to right shoulder.
(4) Red light to right of green light.
(5) Red vertical line (light) seen tilted, top to (patient's) left.

Interpretation and Tabulation of Findings (*Fig.* 2).

Test 1.—This shows right eye higher, left eye lower. This may be due to spasm of the right elevators or to paralysis of the right depressors, so we place on line 1, Fig. 2, S at the right elevators and P at the right depressors. The condition may also be due to spasm of the left depressors or to paralysis of the left elevators. So we place on same line, S at the left depressors, and P at the left elevators.

Test 2.—The muscles which have their greatest vertical action down and left are the right superior oblique and the left inferior rectus (Fig. 2); the limbs are like windows facing in the direction of the field of greatest " down " action of these muscles. Since the vertical diplopia increases in this direction, there may be a paralysis of either of these muscles or a spasm of their direct antagonists. So we place on line 2, P at the right superior oblique and the left inferior rectus, and S at the right inferior oblique and the left superior rectus. The corresponding muscles on the right side of each ring are " neutral " in this movement, so we place a dot (·) at each of these, the right superior rectus, the right inferior rectus, the left inferior oblique, and the left superior oblique.

Test 3.—This shows that any of the muscles which normally produce compensatory *levo-torsion* may be incapable of doing so (*i.e.* paralysed), or that their antagonists are spastic. The laevo-torting muscles as seen on the schema are (in the right eye), the right superior rectus and the right inferior oblique, and (in the left eye) the left inferior oblique and the left inferior rectus. So we place on line 3, P at each of these muscles, and S at their antagonists, that is, at the right inferior oblique, the right inferior rectus, the left superior rectus, and the left superior oblique respectively.

Test 4.—This shows esotropia (homonymous diplopia), which may be caused by spasm of any of the vertical adductors, the vertical recti on the outside of each ring, or paralysis of any of the vertical abductors, the obliques, on the inside of each ring. So we place on line 4, S at each of the vertical recti and P at each of the obliques.

Test 5.—The tilt of the right-eye image points to paralysis of either muscle in the right eye attached to a limb tilted to the left (the tilt of the false image is the same as the torsion of the paralysed muscle shown by the tilt of the limb in the schema); so we place on line 5, P at the right superior rectus and the right superior oblique. Or the tilt of the image may be due to spasm of the antagonists of the aforementioned muscles; so we place on line 5, S at the right inferior oblique and the right inferior rectus. The muscles in the left eye (which sees the straight-line image) are "neutral", so we place a dot (·) on line 5 at these muscles.

Diagnosis.—We see here an agreement or concordance of the same letter P (five Ps) at the right superior oblique. We therefore have paralysis of the right superior oblique, left eye fixing.

Case 2, Tests and Findings

(1) Red light higher green light lower.
(2) Vertical separation of images greatest up and left.
(3) Vertical separation of images increases on tilting head to left shoulder.
(4) Red light seen to left of green light (crossed diplopia).
(5) Red linear line (light) seen tilted, top to (patient's) right.

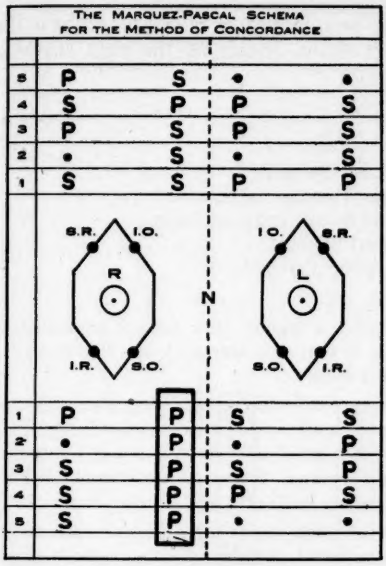

FIG. 2.—Case 1, paralysis of right superior obique, left eye fixing.

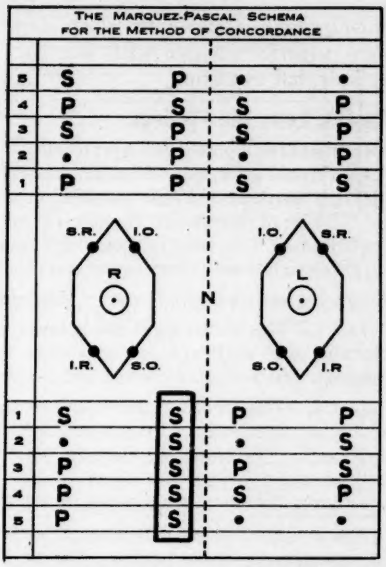

FIG. 3.—Case 2, spasm of right superior oblique, left eye fixing.

Interpretation and Tabulation of Findings (*Fig.* 3).

Test 1.—This shows right eye lower. This may be due to paralysis of either elevator of the right eye or to spasm of either depressor of the right eye. So we place on line 1 (Fig. 3), P at the elevators of the right eye and S at the depressors of the right eye. Or as the left eye is higher we may have spasm of the left elevators or paralysis of the left depressors. So we place on line 1, S and P at these muscles, respectively.

Test 2.—This shows possible paralysis of the muscles whose greatest field of up action is up and left. This points to the right inferior oblique or the left superior rectus (Limbs like windows face up and left to fields of greatest action). So we place on line 2, P at these muscles. Or either of the antagonists of these muscles may be in spasm. So we place on line 2, S at the right superior oblique and the left inferior rectus. We place a dot (·) at the muscles on the right side of each ring as they are "neutral" in this movement.

Test 3.—This shows possible paralysis of the dextro-tortors of either eye or spasm of the laevo-tortors of either eye. We therefore place on line 3 P at the dextro-tortors of the right eye, the right inferior oblique and the right inferior rectus, and S at their antagonists, the right superior rectus and the right superior oblique. We also place P at the dextro-tortors of the left eye, the left superior rectus and the left superior oblique, and S at their antagonists, the left inferior oblique and the left inferior rectus.

Test 4.—Crossed diplopia shows exotropia. This may be due to spasm of the abductors or to paralysis of the adductors. So we place on line 4 P at the vertical recti of both eyes, and S at the obliques of both eyes.

Test 5.—This shows torsion of the right eye. Tilt of the image is the same as slant of limb of paralysed muscle. This may be either the right inferior oblique or the right inferior rectus, so we place on line 5 P at the right inferior rectus and the right inferior oblique. Or it may be due to spasm of their torsional antagonists, so we place S at the right superior rectus and the right superior oblique. We place dots (·) at the corresponding muscles on the left ring.

Diagnosis.—The muscle which shows the greatest degree of concordance is the right superior oblique with five Ss. This shows spasm of the right superior oblique, left eye fixing.

Case 3, Tests and Findings.

(1) Red light higher green light lower.
(2) Vertical separation of images greatest down and right.
(3) (*a*) Head tilted to right shoulder, no change in position of lights.
(*b*) Head tilted to left shoulder, lights move further apart vertically.
(4) Red light to right of green light (uncrossed diplopia).
(5) Green line seen tilted, upper end tilted to (patient's) right.

Interpretation and Tabulation of Findings (Fig. 4).

Test 1.—This shows right eye is lower and left eye higher. For reasons explained in previous cases we therefore place on line 1 (Fig. 4) P at right elevators, and S at right depressors, also S at left elevators and P at left depressors.

Test 2.—This direction down and to the right points to the field of greatest (down) action of right inferior rectus and left superior oblique (at " windows " facing that direction). Therefore, we place on line 2, P at right inferior rectus and left superior oblique, and S at their vertical antagonists, right superior rectus and left inferior oblique. We place a dot (·) at the muscles on the left, as they are " neutral " in this movement.

Test 3.—This shows that there is weakness or paralysis of the muscles which cause (compensatory) dextro-torsion. We place P on line 3 at these muscles on both rings, right inferior rectus and right inferior oblique, and left superior rectus and left superior oblique. Or there is spasm of their torsional opponents (*i.e.* the muscles that produce laevo-torsion), so we place on line 3, S at right superior oblique and right superior rectus, and left inferior oblique and left inferior rectus.

Test 4.—This shows esotropia (uncrossed diplopia) due either to a spasm of the vertical adductors (vertical recti of both eyes) or to a paralysis of the vertical abductors (obliques of both eyes). We therefore place on line 4, S at the vertical recti of both eyes and P at the obliques of both eyes.

Test 5.—The torsion of the false image is the same as the slant of the limb for the paralysed muscle. It really corresponds to the torsion produced by that muscle when normal. Therefore, dextro-torsion of the image of the left eye may be due to paralysis of the dextro-torting muscles in the left eye, left superior rectus or left superior oblique, the limbs which slant to the right. We therefore place on line 5 P at left superior rectus and left superior oblique. Or the condition may be due to spasm of their torsional opponents, left inferior oblique and left inferior rectus, so we place S on line 5 at these muscles. We also place a dot (·) on line 5 at each of the muscles of the right eye as this eye shows no torsion.

Diagnosis.—We see here that the muscle which shows the greatest degree of concordance (concurrence or agreement) of the same symbol (P) is the left superior oblique, with five Ps. We therefore have here a paralysis of the left superior oblique, right eye fixing.

Case 4, Tests and Findings.

(1) Red light lower than green light.
(2) Vertical separation of images greatest up and left.
(3) Patient does not notice increased vertical separation of images on tilting head to either shoulder.
(4) Red light to left of green light (test made in right side of field).
(5) Green tubular light tilted to right (test made in right side of field).

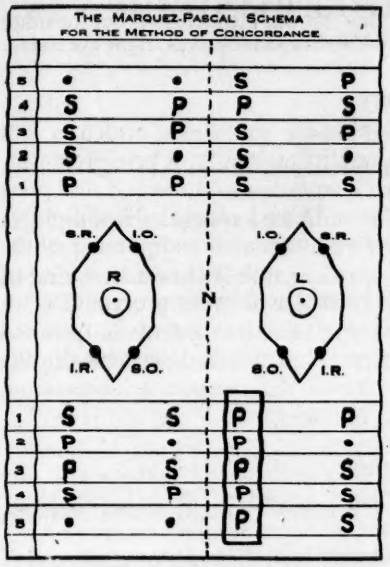

FIG. 4.—Case 3, paralysis of left superior oblique, right eye fixing.

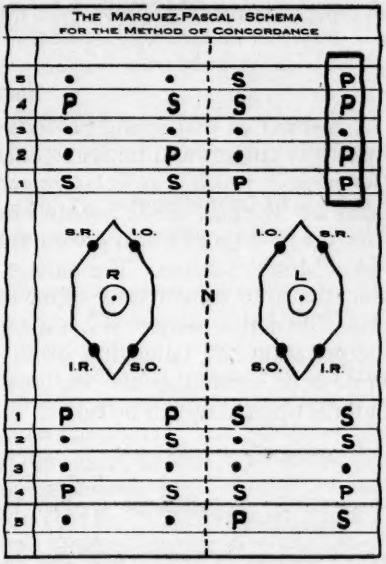

FIG. 5.—Case 4, paralysis of left superior rectus, right eye fixing.

Interpretation and Tabulation of Findings (*Fig. 5*).

Test 1.—This shows right eye is higher and left eye lower. We therefore place on line 1 S at right elevators, and P at right depressors. We also place P at left elevators and S at left depressors.

Test 2.—This direction shows the field of greatest up action of the right inferior oblique and the left superior rectus. The increased vertical separation of the images in that direction may be due to paralysis of the right inferior oblique or the left superior rectus, or to a spasm of their vertical opponents, the right superior oblique and the left inferior rectus. We therefore place on line 2 P at the former and S at the latter muscles. We place a dot (·) at the muscles on the right side of each ring.

Test 3.—This shows no apparent anomaly of any of the muscles. It may be noted, however, that the effect of tilting the head to either shoulder is more marked in paralysis of an oblique muscle than in paralysis of a rectus muscle. So we place a dot (·) on line 3, above and below the rings, at all the muscles.

Test 4.—This shows exotropia which may be due to spasm of the vertical abductors or to paralysis of the vertical adductors. So we place on line 4 S at the obliques and P at the vertical recti.

Test 5.—Shows torsion (laevo-torsion) of the left eye. The tilt of the image is like the slant of the limb of the paralysed muscle (or opposite to the torsion of the eye). The paralysed muscle may therefore be the left superior rectus of the left superior oblique, and we place on line 5 P at these muscles. Or it may be caused by a spasm of the torsional antagonists of these muscles, so we place S at the left inferior oblique and the left inferior rectus. We place dots (·) at the corresponding muscles on the right ring.

Diagnosis.—The muscle which shows the greatest degree of concordance is the

left superior rectus with four Ps and a dot. One test was inconclusive, but the other tests show that we have here a paralysis of the left superior rectus, right eye fixing.

Summary

A method of diagnosing paralytic and spastic strabismus, which is still practically unknown to English-speaking ophthalmologists, is here presented. The method, which is an enlargement and adaptation of a method first presented by Marquez (1942), comprises a co-ordinated system of five diplopia tests, the findings of which are interpreted and tabulated with the aid of the Pascal Muscle Schema. The paretic or spastic muscle is shown by a kind of concurrence or concordance of the same symbol used in the process of tabulation. In actual practice it is not necessary to separate the findings from the interpretation and tabulation on the schema, but this is done here for the purpose of facilitating the exposition. Once the method is understood, all three operations can be carried out in one step.

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STEREOSCOPIC VISION IN RELATION TO PHOTO-INTERPRETATION*

BY

ALAN A. MORGAN

Dagenham, Essex

SINCE the intelligence reports issued during the war depended partly on the proper interpretation of operational photographs, this subject acquired considerable importance.

The final report on an operational photograph depends on several qualities of the interpreter, particularly his specialized knowledge of the subject and his stereoscopic sense.

Stereoscopic vision or depth perception is a distinct property of the cones of the fovea and is dependent on the stimulation of disparate points in the retinae. Generally, one utilizes associated factors (*e.g.* size, shadows, etc.), in determining the position of objects in space, so that true stereoscopic sense is not really developed in the average person.

An attempt has been made to determine the value of stereoscopic training in photo-interpretation and to ascertain the effect of suppression changes and refractive errors on stereoscopic vision.

Method

As many personnel as possible were graded stereoscopically and then divided into two groups. One group were stereoscopically trained and the others acted as controls. The grading and training were carried out on Holmes' stereoscopes with the rotating stereograms of Livingston (1939). The initial grading was done on Charts 1 and 5, a note of any abnormality in convergence or simultaneous perception being made at the time. The training was carried out progressively on Charts 4, 6, 10, 9, and 7. At the end of the training period, the trainees were examined with their controls (as far as possible the controls had an original grading similar to the trainees). The final test was carried out on Charts 5 and 8 of the series and also on an operational photograph. Chart 5, which is a difficult one, and on which the initial grading was done, enables one to see what improvement the training has had on their stereoscopic sense. Chart 8 had not been seen previously by either the trained or untrained personnel. The operational photograph chosen for the final test had particular stereoscopic properties, so that, if only associated factors were utilized in depth perception, wrong conclusions might be drawn, and the exercise of true stereoscopic vision was needed for its accurate interpretation.

The trained personnel went through a graduated course of twenty sessions on Charts 4, 6, 10, 9, and 7—an average session lasting 10–15 minutes.

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TABLE I. EFFECT OF TRAINING ON STEREOSCOPIC VISION

No.	Age	Previous Occupation	Visual Acuity		Convergence	Simultaneous Perception	Stereoscopic Vision		No. of Sessions	Final Test		
			Without Glasses	With Glasses			Initial Grading			Chart 8 per cent.	Chart 5	Op. Photo. per cent.
							Chart 1	Chart 5				
Subject 1	39	Schoolmaster	6/5 6/5	—	Normal	Normal	213	A.1.B.3. C.2.D.4.	17	70	A.1.B.3. C.2.D.4.	80
Control 1	35	Museum curator	6/5 6/5	—	Normal	Normal	213	A.1.B.3. C.2.	—	70	A.1.B.3.	100
Subject 2	31	University lecturer	6/60 6/60	6/6 6/6	Normal	Normal	231	Nil	22	50	A.1.B.3. C.2.D.4.	85
Control 2	29	Schoolmaster	6/9 6/6	6/6 6/6	Normal	Normal	213	A.1.	—	40	A.1.B.3. C.2.	80
Subject 3	22	Art student	6/5 6/5	—	Normal	Normal	213	A.1.B.2.	16	60	A.1.B.3. C.2.D.4.	70
Control 3	30	Quantity surveyor	6/6 6/6	6/5 6/5	Normal	Normal	231	Nil	—	50	Nil	70
Subject 4	22	Silversmith	6/24 6/18	6/6 6/6	Normal	Slight suppression left	213	A.1.B.3.	18	50	A.1.B.3. C.2.D.4.	75
Control 4	33	Schoolmaster	6/5 6/5	—	Normal	Normal	213	A.1.B.3.	—	80	A.1.B.3.	85
Subject 5	35	Artist	6/5 6/5	—	Normal	Normal	213	A.1.B.3.	15	80	A.1.B.3. C.2.D.4.	100
Control 5	35	Schoolmaster	6/5 6/5	—	Normal	Normal	213	A.1.B.3. C.2.	—	40	A.1.B.3. C.2.D.4.	90
Subject 6	29	Geologist	6/5 6/5	—	Normal	Normal	213	A.1.B.3. C.2.	28	80	A.1.B.3. C.2.D.4.	100
Control 6	34	Schoolmaster	6/6 6/6	—	Normal	Normal	213	A.1.B.3. C.2.	—	80	A.1.B.3. C.2.	100
Subject 7	25	Railway official	6/6 6/6	—	Normal	Normal	213	A.1.B.3.	21	90	A.1.B.3. C.2.D.4.	100
Control 7	38	Bookseller	6/9 6/12	6/6 6/6	Normal	Normal	213	A.1.B.3.	—	60	A.1.B.3. C.2.D.4.	100
Subject 8	20	Nil	6/6 6/6	—	Normal	Some suppression right	213	Nil	24	70	A.1.B.3.	80
Control 8	29	Teacher	6/5 6/5	—	Normal	Slight suppression right	213	Nil	—	40	Nil	50

Owing to shift work and other factors it actually took 3 or 4 months to complete a course, and throughout this time both the trainees and their controls were actively engaged in photo-interpretation. To enable the results to be understood, it may be pointed out that the correct answers to Charts 1 and 5 are 213 and A.1.B.3.C.2.D.4. respectively.

Results

Effect of Training (Table I).

The number of personnel concerned is too small to draw very definite conclusions, but the Table suggests the following points:

(*a*) All the trained personnel show a definite improvement on Chart 5 after their course of training.

(*b*) The majority of untrained personnel show little or no improvement on Chart 5.

(*c*) On the operational photograph there seems very little to choose between trained and untrained personnel, but, on the whole, the trained did a little better.

These points indicate that a definite improvement in stereoscopic vision results from steresocopic training. Furthermore, it appears that personnel engaged on stereoscopic work have their stereoscopic vision automatically improved without undergoing any special stereoscopic training, although this happens more slowly than with systematic graduated training. It is felt that even better results could be produced in the trained candidates if the training sessions had been on consecutive days, and that a greater contrast would then have been evident between the trained and untrained personnel on the operational photograph as well, as after only 3 weeks (the time needed for a concentrated course of training) the untrained personnel would not have been carrying out their daily work long enough to make any appreciable improvement in their stereoscopic vision.

Effect of Suppression Changes (Table II).

Section A contains subjects with complete or nearly complete suppression

TABLE II

Section	No.	Age	Convergence	Simultaneous Perception	Stereoscopic Vision		After a Course of Training			
					Chart 1	Chart 5	Chart 1	Chart 5	Chart 8 per cent.	Op. Photo per cent.
A	1	55	Normal	Complete suppression left	123	Nil	123	Nil	10	0
	2	38	Normal	Complete suppression left	Nil	Nil				
	3	19	Normal	Considerable suppression right	123	Nil				
B	4	37	Normal	Some suppression right	213	Nil				
	5	35	Normal	Normal	213	A.1.B.3.C.2.				
	6	40	Normal	Some suppression right	123	Nil				
	7	34	Normal	Normal	213	A.1.B.3.C.2. D.4.				
	8	36	Normal	Some suppression right	231	A.1.				
	9	29	Normal	Normal	213	A.1.B.3.C.2.				
C	10	20	Normal	Some suppression left	213	Nil	213	A.1.B.3.		
	11	29	Normal	Some suppression right	213	A.1.B.3.C.2.	213	A.1.B.3. C.2.D.4.		

of one eye and it is seen that they exhibit no stereoscopic sense. Subject No. 1 was given a trial of 7 days' continuous training, but not the slightest improvement in his suppression or stereoscopic sense could be detected.

Section B compares those with partial suppression and those with no suppression. It illustrates that the cases of partial suppression have worse stereoscopic vision than the others.

Section C shows the effect of exercises on those with partial suppression and suggests that they may be amenable to training. Incidentally, these two candidates required the most sessions to complete their training (28 and 24 respectively), exercises to overcome suppression being necessary before stereoscopic training could be begun.

Generally, therefore, those with complete or nearly complete suppression are unsuitable for photo-interpretation. Those that show partial suppression should only be accepted for the work as second choice after those who show no suppression, and then only after a week's trial to find out whether they are amenable to training. If they are, they should then undergo a complete course of stereoscopic training.

Effect of Refractive Errors (Tables III, IV, V, and VI).

Table III shows subjects with refractive errors but good stereoscopic vision, and Table IV those with refractive errors but poor stereoscopic vision. The fact that Subject No. 6 developed satisfactory stereoscopic vision after training suggests that refractive error is no handicap to successful stereoscopic training.

TABLE III

No.	Age	Convergence	Simultaneous Perception	Stereoscopic Vision		Visual Defects
				Initial Grading		
				Chart 1	Chart 5	
1	21	Normal	Normal	213	A.1.B.3.C.2.D.4.	Mild hypermetropic astigmatism
2	34	Normal	Normal	213	A.1.B.3.C.2.	Mild hypermetropic astigmatism
3	20	Normal	Normal	213	A.1.B.3.C.2.	Hypermetropic astigmatism
4	36	Normal	Normal	213	A.1.B.3.C.2.	Myopic astigmatism especially right eye
5	35	Normal	Normal	213	A.1.B.3.C.2.	Moderate myopia
6	23	Normal	Normal	213	A.1.B.3.C.2.D.4.	Hypermetropic astigmatism
7	25	Normal	Normal	213	A.1.B.2.C.3.D.4.	Hypermetropic astigmatism
8	32	Normal	Normal	213	A.1.B.3.C.2.D.4.	Severe myopia. Visual Acuity less than 1/60 in each eye

TABLE IV

No.	Age	Convergence	Simultaneous Perception	Stereoscopic Vision		Final Grading			Visual Defects
				Initial Grading		Chart 8 per cent.	Chart 5	Op. Photo per cent.	
				Chart 1	Chart 5				
1	34	Normal	Normal	213	Nil				Myopic astigmatism
2	20	Normal	Normal	213	Nil				Myopia+++
3	26	Normal	Normal	213	Nil				Moderate myopia
4	30	Normal	Normal	231	Nil				Hypermetropic astigmatism
5	35	Normal	Normal	213	Nil				Hypermetropic astigmatism (both eyes)
6	31	Normal	Normal	231	Nil	50	A.1.B.3. C.2.D.4.	85	Myopia+++

Table V shows subjects with normal visual acuity and good stereoscopic vision, and Table VI those with normal visual acuity but poor stereoscopic vision.

TABLE V

No.	Age	Convergence	Simultaneous Perception	Stereoscopic Vision		Visual Defects
				Initial Grading		
				Chart 1	Chart 5	
1	20	Normal	Normal	213	A.1.B.3.C.2.D.4.	Nil
2	28	Normal	Normal	213	A.1.B.3.C.2.	Nil
3	31	Normal	Normal	213	A.1.B.3.C.2.D.4.	Nil
4	48	Normal	Normal	213	A.1.B.3.C.2.D.4.	Nil
5	24	Normal	Normal	213	A.1.B.3.C.2.D.4.	Nil
6	30	Normal	Normal	213	A.1.B.3.C.2.D.4.	Nil
7	27	Normal	Normal	213	A.1.B.3.C.2.D.4.	Nil
8	18	Normal	Normal	213	A.1.B.3.C.2.D.4.	Nil

TABLE VI

No.	Age	Convergence	Simultaneous Perception	Stereoscopic Vision		Visual Defects
				Initial Grading		
				Chart 1	Chart 5	
1	26	Normal	Normal	213	A.1.	Nil
2	33	Normal	Normal	213	Nil	Nil
3	33	Normal	Normal	213	Nil	Nil
4	24	Normal	Normal	213	Nil	Nil
5	34	Normal	Normal	231	A.1.B.3.	Nil
6	24	Normal	Normal	213	A.1.	Nil
7	22	Normal	Normal	231	A.1.	Nil
8	21	Normal	Normal	213	Nil	Nil
9	41	Normal	Normal	213	A.1.	Nil
10	29	Normal	Normal	213	Nil	Nil
11	22	Normal	Normal	213	Nil	Nil

These results show that there is no correlation between refractive errors and stereoscopic vision.

Conclusions

It has been noticed that it is not uncommon for personnel to complain of ocular symptoms such as tiredness of the eyes and headaches after beginning to use the stereoscope in photo-interpretation. This is merely due to ocular fatigue, probably resulting from the fact that the ideal way of looking at a photograph is to dissociate accommodation from convergence. This, plus the bending over whilst looking at photographs with its associated increased intra-ocular tension and impaired intra-cranial venous drainage is probably responsible for the symptoms. They usually wear off in a week or two.

Stereoscopic work *per se* has no evil effects on the eyes, and there is no reason at all why any refractive errors already present should be increased as a result of the stereoscopic work, providing it is done under proper conditions, especially with adequate lighting and good arrangements of desks and chairs. It is recommended that there should be a uniform illumination of the whole operational room, plus a slightly greater illumination of the photograph under observation. There should not be much contrast between the illumination on the photograph and the surroundings, as adaptation changes would then come into play and might produce further symptoms. It is also recommended that the ledge of the desk on which the operational photograph rests for stereoscopic examination should be far more vertical than that in general use.

As regards standards for recruits undertaking photo-interpretation, it seems that suppression changes are far more important than visual acuity, and since the type of person often found suitable for the work is of the academic class, it is not uncommon to find refractive errors present.

The following standards are recommended:

1. *Visual Acuity.*—6/60 or better in each eye, correctable to 6/6.
2. *Convergence.*—4″ or better.
3. No cases of complete suppression should be accepted.
4. Cases with partial suppression should only be accepted with the aforementioned proviso (Table II).

As regards those who may be particularly well qualified for photo-interpretation, the standard may be relaxed in regard to visual acuity after testing their stereoscopic vision, but not in regard to suppression changes.

It is also recommended that all personnel, irrespective of their initial grading, should have a complete course of stereoscopic training with daily exercises.

I wish to thank Air Marshal Sir P. C. Livingston, K.B.E., C.B., A.F.C., formerly Consultant in Ophthalmology, Royal Air Force, for his help and interest in this work.

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HISTOCHEMICAL LOCALIZATION OF ALKALINE PHOSPHATASE IN THE RETINA*

BY

J. L. REIS

Postgraduate Medical School, London

CHEMICAL investigations have shown that alkaline phosphatase is present in the retina (De Conciliis, 1934; Reis, 1951). In these investigations the whole retina was homogenized and the enzyme estimated in extract. Obviously the estimations of enzyme activity by such a necessarily gross method give no idea of the exact distribution of the enzyme in this, functionally, so finely differentiated tissue. This object may only be achieved by using histochemical methods. A knowledge of the histological localization of the phosphatase in the retina, may perhaps enable us to make some suggestions about its physio logical role there.

Gomori (1939) described a method of demonstrating alkaline phosphatase activity in tissue slides. This method consists in incubating the fixed tissue slides with buffered solution of a phosphate ester and a calcium salt. The phosphatase hydrolyses the ester, and the liberated phosphate forms a precipitate of calcium phosphate. The latter is converted to cobalt phosphate (by the addition of cobalt nitrate solution) and this with ammonium sulphide produces black, insoluble, cobalt sulphide. Thus black deposits of cobalt sulphide are formed at the sites of phosphatase activity.

This technique was used by Süllmann and Payot (1949) in the study of corneal epithelium phosphatase. François and Rabaey (1951), and simultaneously De Vincentiis (1951), published their investigations on the phosphatase activity of different ocular tissues. Since in the described method phosphatase activity is visualized as a brown or black deposit, it is difficult to differentiate it from the similarly coloured melanin pigment. Francois and Rabaey comment on this difficulty in their paper. They make the final observations by comparing the phosphatase-stained slides with control slides. If melanin is present in the control, the activity of phosphatase is demonstrated when a darker or more abundant staining seems apparent in the incubated slide. De Vincentiis (1951) found another solution to this problem. For the study of phosphatase in uveal membranes he used albino rabbits—thus avoiding the presence of melanin, but limiting his research to these animals only.

The disadvantage of the method used in these papers is that calcium phosphate is not wholly insoluble but is apt to be diffused to a certain extent. As a result, deposits may occur which are not a true indication of phosphatase activity. There also exists a tissue affinity for cobalt salts, so that the cobalt

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salts may not only react with the calcium phosphate but may also be attached directly to some tissue structures. In order to avoid these difficulties, Gomori (1951) devised a new method of phosphatase staining, subsequently modified by Grogg and Pearse (1952). This new method consists in using α-naphthyl-phosphate in the presence of a diazonium compound. The α-naphthol produced by the phosphatase hydrolysis forms a diazo-dye with the diazonium compound. If the diazotate of 5-chloro-*o*-toluidine is used, the resulting diazo-dye is red and easily differentiated from the melanin pigment. It does not diffuse so easily as calcium phosphate. If this method is used, the nuclei usually do not stain. This suggests that what was previously often described as nuclear phosphatase, was an artefact, due most probably to the diffusion of calcium phosphate.

In all previous papers dealing with histochemistry of eye-tissue phosphatases, the Gomori's first method was used and a great deal of nuclear staining was observed. It therefore seemed that it could be of interest to apply this new method to eye tissues, in this way excluding the diffusion of calcium phosphate and the unspecific cobalt staining, and giving the resulting deposits a different colour from that of the melanin pigment.

Method

Gomori's method was used for tissue fixation (cold acetone) and for the preparation of slides as described by Pearse and Reis (1952). The slides were incubated by the method of Grogg and Pearse (1952) and Pearse (1953) at room temperature for 15 to 30 min. in freshly-made solution containing 1 mg. sodium *α-naphthylphosphate* and 1 mg. 5-chloro-*o*-toluidine diazotate per 1 ml. m/20 veronal buffer (*p*H 9).

Some slides were stained using for comparison Gomori's phosphatase method (calcium phosphate-cobalt sulphide).

Results

For comparison a slide of bovine retina was stained by Gomori's phosphatase method (Fig. 1).

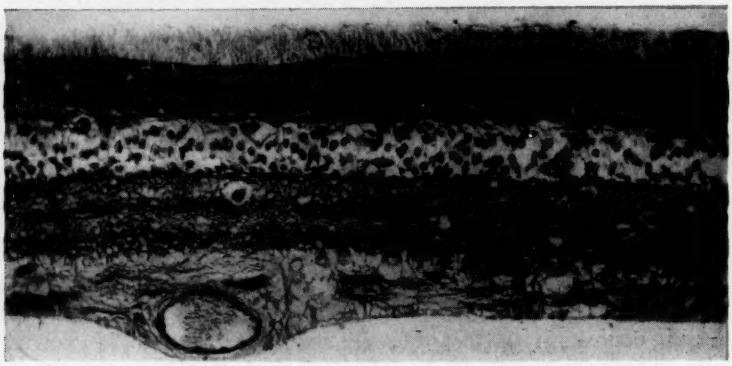

FIG. 1.—Alkaline phosphatase in bovine retina using the calcium phosphate—cobalt sulphide method. ×190.

Fig. 2 shows a serial slide of the same retina stained by the new diazo-dye phosphatase method. The difference is clear, whereas the old method shows extensive staining of the nuclei in addition to staining of the vascular endothelia and of the plexiform layers; in the diazo-dye method only the vascular endothelia are well stained, the plexiform layers show a very slight reaction, and the nuclei do not stain at all.

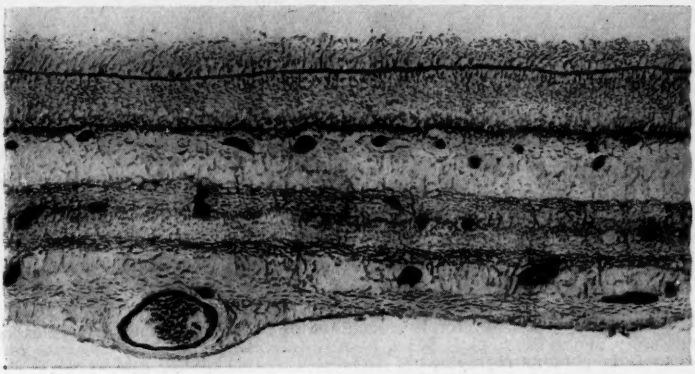

FIG. 2.—Alkaline phosphatase in bovine retina using the diazo-dye method. ×190.

Conclusions

François and Rabaey (1951) and De Vincentiis (1951), studying the histological localization of alkaline phosphatase, show very marked staining of nuclei. As they were using Gomori's method, which he himself (Gomori, 1951) later decided was not very accurate, it is probable that their results were affected by the calcium phosphate diffusion. The nuclei in general have affinity for different substances, *e.g.* dyes such as methylene blue. The affinity of nuclei for the calcium phosphate is probably of a similar kind. The final cobalt sulphide deposits do not correspond here exactly to the sites of phosphatase activity. The diazo-dye method seems to be much more selective and freer from diffusion phenomena, and its results seem more reliable than those obtained by the older methods.

The staining of the vascular endothelium in the retina, using the alkaline phosphatase diazo-dye method, is so sharply defined that it seems to be possible to apply it to the study of the anatomy and pathology of the retinal vessels.

Some earlier writers, basing their observations of the phosphatase activity in the retina on chemical estimations, suggested that the alkaline phosphatase in the retina may play a role in phosphate metabolism connected with photochemical reactions. In view of the histological localization of phosphatase, this does not seem possible, all the enzyme being concentrated in the inner walls of the vessels.

It seems worth mentioning here that a highly active alkaline phosphatase is present in the whole uveal membrane and in the choroid plexus. These tissues play some part in the formation of the intra-ocular and cerebrospinal fluids, in that they regulate to a certain degree the passage of ions. It follows that the alkaline phosphatase probably has a role in regulating the phosphate ion concentrations. The site of its activity in the eye corresponds to the hypothetical " blood-aqueous barrier ".

Summary

(1) Alkaline phosphatase localization in the retina was studied by the diazo-dye coupling method.

(2) Alkaline phosphatase in the retina was found mainly in the vascular endothelium, only a very slight reaction being shown by the plexiform layers.

(3) The extensive staining of retinal nuclei when Gomori's phosphatase method (calcium phosphate-cadmium sulphide) is used, is an artefact due to calcium phosphate diffusion.

I wish to express my thanks to Prof. E. J. King for the opportunity to perform the experiments n his laboratory, and to Dr. A. G. E. Pearse for his advice and the necessary reagents. Mr. E. W. Willmott took the photomicrographs.

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EXENTERATION OF THE ORBIT*
AND USE OF ALGINATE MOULD FOR APPLYING SKIN GRAFTS

BY

JEAN M. DOLLAR AND MARY SAVORY

Royal Eye Hospital, London

CLASSICAL descriptions of exenteration depict it as a swift and sanguinary procedure. Modern methods of anaesthesia and the introduction of diathermy coagulation have made a more exact dissection possible, so that the main interest of the operation now centres in the after-treatment of the cavity. However, it seemed worth while to describe the operation itself, with emphasis on practical details culled from the standard descriptions and from our own experience.

(A) GENERAL CONSIDERATIONS

(1) Conservation or Removal of the Lids.—When it is consistent with the complete removal of all malignant disease, the lids can be conserved, and either turned into the cavity to assist its epithelialization or used to retain a prosthesis. We have not had experience of these procedures, but those who have stress the tendency of the lids to shrink and cause difficulties. Their removal is certainly no obstacle to the fitting of an efficient prosthesis, and simplifies both the operation and the management of the cavity.

(2) Skin Grafting the Cavity.—This is advisable if there are no surgical contra-indications. Without it, the cavity granulates, and is slowly epithelialized from the skin margins, meanwhile requiring regular dressings, and producing a discharge which is often offensive and distressing to the patient. The cavity may be grafted immediately, but this involves placing the graft on bare bone, and its blood supply is necessarily precarious. With the aid of antibiotics it is possible to keep the cavity aseptic, and to delay grafting until granulations cover a large part of its walls, usually at the end of 2 weeks. The graft then takes very well.

(3) Method of Applying the Graft.—The success of a skin graft depends mainly on the whole surface being held in contact with the receptor area by firm even pressure. In a hard-walled cavity like the orbit, this is best achieved by making a mould in the cavity. Since the anterior orbital margins overhang its walls, any complete mould must have considerable elasticity if it is to be taken out, draped with the graft, and reinserted. Such a mould can be made from alginates. Sodium alginate is supplied as a sterile syrup-like solution which sets to a jelly on the addition of calcium chloride solution. This jelly is toughened by incorporating in it calcium alginate wool, which resembles ordinary cotton wool. A trial run in a cocktail glass gives a good idea of the behaviour of the materials.

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(B) Exenteration

(1) Incision.—The lids are stitched together. As the skin is easily displaced over the bone, the bony landmarks are palpated, and the line of the desired incision marked out with gentian violet or with dots of diathermy coagulation. Unless the extent of the disease makes it necessary to do otherwise, the line of the incision lies just inside the orbital margin above and below. Medially it lies on the anterior lacrimal crest, and laterally it passes close to the outer canthus. Care should be taken, when making the join between the upper and lower incisions, to avoid carrying the ellipse too far laterally, for when the skin retracts a small triangle of malar bone is exposed. This is very slow to be covered by granulations or skin, and healing is therefore delayed. If the incision round the orbit is too small to allow easy access to the deeper layers, a straight horizontal incision can be made outwards and closed at the end of the operation.

(2) Dissection.—The incision is carried down to the bony margin all round. It is convenient to start at the lower end of the lacrimal crest, to continue the incision below and up towards the outer canthus, and to make the incision above at the last so that blood from it does not obscure the view. Bleeding points are picked up with artery forceps, and coagulated in batches by touching the forceps with the diathermy coagulating terminal. Ligature may be required for a few of the larger arteries.

The periosteum is best incised a few millimetres outside the orbit, rather than on the orbital margin, as the blade of the knife can then be used perpendicularly to the bone. Although the periosteum here is firmly adherent to the bone, it is thick, and does not tear easily when raised. The dissection is begun at the upper outer quadrant, and once between periosteum and bone it is easy to keep in this plane. Freer's nasal raspatories, sharp and blunt, have proved very convenient as they have the right curve for orbital work. After incising the periosteum, the sharp raspatory is used to raise it from the bone, and to separate it as far as the orbital margin. Provided it is not involved in malignant disease, the periosteum strips easily in the orbital cavity using the blunt raspatory and gauze dissection.

The periosteum is adherent at the attachment of the pulley of the superior oblique muscle, and the attachment must be cut, avoiding damage to the roof of the orbit, which may be thin. On the nasal wall of the orbit the periosteum must be raised gently, for the orbital plate of the ethmoid is often very fragile and a sinus may result if the ethmoid air cells are opened. As the periosteal incision is made in the region of the anterior lacrimal crest, the lacrimal sac is reflected laterally with the orbital contents when the periosteum is separated from the nasal wall. The naso-lacrimal duct is identified as the dissection proceeds from the nasal wall to the floor of the orbit. Ligation of the duct has the advantage of preventing ascending infection from the nose, and of stopping blood running down into the nasopharynx. In the floor of the

orbit periosteal bands passing into the inferior orbital fissure may need to be divided, care being taken to avoid damaging the structures in the fissure. Laterally the temporal and malar branches of the lacrimal artery enter the malar bone, and medially the anterior ethmoidal artery passes from the orbit into the anterior ethmoidal foramen. These vessels are exposed as they pass between periosteum and bone, and if they are clamped and coagulated with diathermy, tiresome bleeding in the depths of the wound is avoided. The periosteum is stripped as far back towards the apex of the orbit as possible.

The shape of the apex of the orbit varies surprisingly, as one finds if one tries possible pedicle clamps in different skulls. It is therefore wise to have a selection of the larger curved artery forceps and to choose the best for use at the time. Most cases require a medial and a lateral clamp, but the exact angle at which they fit best varies. The two clamps are applied as far back as possible, and it is usually advised that two lighter ones be applied in front of them, but the second pair of clamps may tear the periosteum, and make it more difficult to remove the mass cleanly. The pedicle is divided in front of the deep pair of clamps with curved scissors. One is sometimes disappointed at the bulk of tissue left at the apex. After removal of the orbital contents it may be possible to apply clamps behind those previously used, and to reduce the size of the stump by the removal of more tissue. The pedicle is transfixed and ligated. The orbital walls are examined for any evidence of neoplastic involvement, and any diseased bone is chiselled away, cutting through healthy bone. If bony involvement is suspected it may be helpful to have the co-operation of an E.N.T. surgeon.

(C) Management of the Cavity

At the end of the operation the cavity is dusted with penicillin powder, lined with tulle gras, and packed with vaseline gauze to which penicillin powder is added. It is important to turn the skin edges in towards the cavity, and to extend the pack over them so that they are firmly pressed against the bone. Broad strips of elastoplast over the dressings help to prevent the skin retracting. Patients have remarkably little pain after exenteration, presumably because all sensory nerves to the area have been cut. The dressings are left undisturbed for a week, when the cavity is inspected and repacked as before, usually (for the patient's peace of mind) under general anaesthesia. At this dressing it is usually possible to decide when the cavity can be grafted; our cases have been ready 2 weeks after exenteration.

(1) **Skin-Grafting the Cavity using an Alginate Mould.**—The mould is prepared in the orbit immediately before cutting the skin graft. The cavity is lined with a square of tulle gras large enough to project over the bony margins. A teaspoonful of the syrup-like alginate is poured in, and pledgets of calcium alginate wool are puddled into this until saturated. Calcium chloride is dripped on to set the mixture, and more sodium alginate and wool are worked in before setting is complete, so as to avoid planes of cleavage. The mould is thus built up by a continuous

process, and the materials are firmly pressed into the periphery of the orbit to fill it accurately. A handle is built into the centre of the mould and projects on the surface. The handle we are at present using is shown in Fig. 1; it consists of a rubber button, threaded with No. 1 black silk; the silk is threaded through a length of fine rubber tubing, which is stiffened by inserting a throat swab stick. The mould is made to fill the orbit, and to overlap its margins for about 2 cm. all round, rising to a dome in the centre. Gentle pressure is thus applied to the whole mould by the dressings. A gentian violet mark is made across the mould and adjacent skin as a guide for reinsertion (Fig. 2). The mould is left in the orbit to consolidate while a Thiersch graft is taken, usually from the inner side of the thigh. The type of Blair's knife with a renewable Gillette blade is convenient for those who do not often cut grafts, as a new blade ensures a perfect edge for each case. Though it is

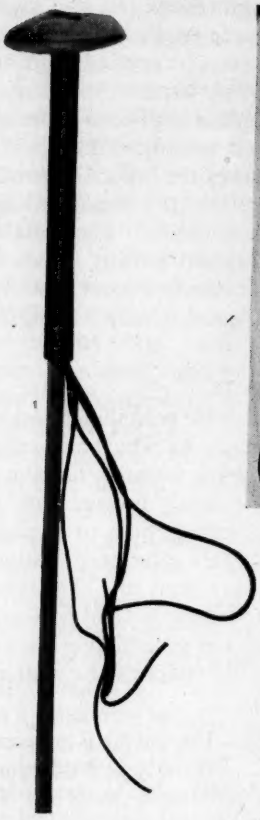

FIG. 1.—Handle for mould (enlarged).

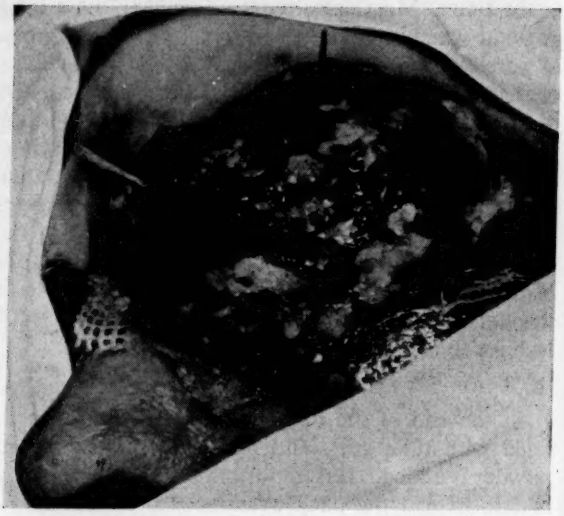

FIG. 2.—Finished mould in orbit. (Note projecting handle and gentian violet mark for orientation).

easier to cover the mould with one piece, two or more pieces of graft can be used if necessary.* The graft is spread out, and turned raw surface downwards on gauze moistened with saline. Alginate gauze has proved a comfortable dressing for the leg wound.

The mould is now removed from the cavity by combined traction on the handle and on the edges of the tulle gras. The tulle gras is removed from the mould, and any breaks, rough places, or cracks in the mould are repaired or smoothed out by putting on sodium alginate and setting it with

* In one case, where it was necessary to use two pieces of graft, the patch was successfully attached to the main graft by using thrombin and fibrinogen as a physiological glue.

calcium chloride. The graft is now draped over and carefully spread out on the mould* (Fig. 3). Moistening the inside of the cavity with fibrinogen and the graft with thrombin immediately before inserting seems to improve the take, but is not essential. The mould is put back into the cavity in exactly its original position, and is pressed firmly home. The skin graft covering the mould is thus held in contact with the whole raw area, and no suturing of the edges is necessary. The mould is covered with a layer of oiled silk or jaconet to prevent drying, and a pressure dressing of cotton wool and elastoplast applied. The handle is now cut short so that it does not protrude beyond the wool.

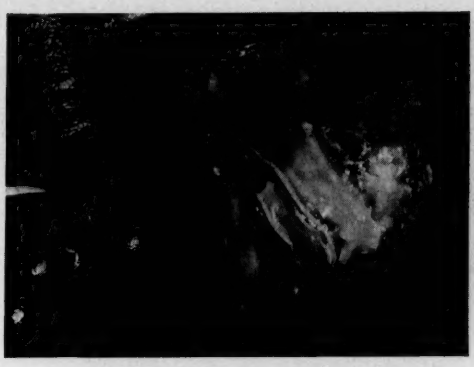

FIG. 3.—Mould draped with skin graft.

(2) After-Treatment.—The mould is removed a week later. The graft now has a milky appearance, which is normal, as its superficial layers usually undergo necrosis, and are shed while the deeper layers survive. There is a frill of dead graft which has overlain the skin round the wound, this is gently cut away, together with any folds of obviously redundant graft. The cavity is lightly packed with vaseline gauze. Hereafter dressings do not need an anaesthetic, and can generally be done at weekly intervals. A change is soon made to dry gauze, as the vaseline makes the skin sodden. Scabs may form in places, and if necessary separation can be hastened by liquid paraffin, or hydrogen peroxide. A prosthesis is fitted as soon as the cavity is healed.

(3) Prosthesis.—Two types are available, and the choice will depend upon the patient's mentality and occupation, and upon the shape of the face.

(*a*) *Spectacle-Attached Prosthesis.*—In this type the prosthesis is attached to the spectacle frame, and moves on and off with it. In presbyopic patients the good eye must be fitted with a bifocal lens to avoid the embarrassment of exposing the empty cavity when changing glasses. The occupation must not be one in which glasses are a nuisance, or are likely to be dislodged (Fig 4*a* and *b*).

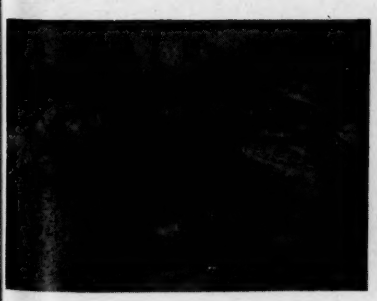

FIG. 4 (*a*).—Patient without prosthesis.

FIG. 4 (*b*).—Same patient with spectacle-attached prosthesis.

(*b*) *Skin-Attached Prosthesis.*—This form fits into the socket, and is stuck to the skin margin by a special non-irritant adhesive; it is removed at night. Any spectacle frames should be made by the prosthesis maker so that they give the best possible effect with the prosthesis. With this type a bifocal lens is not essential and the cosmetic effect is usually better than with the first type, specially if make-up and glasses are worn. The patient, however, must be dextrous enough to apply the prosthesis, and must have sufficient vision in the good eye to do so without a correcting lens (Fig 5*a* and *b*).

FIG. 5 (*a*).—Patient without prosthesis.

FIG. 5 (*b*).—Same patient with skin-attached prosthesis.

DISCUSSION

As an operation for malignant disease, exenteration must be regarded as an unsatisfactory procedure. There is often only a small margin of normal tissue present round the tumour, and the lymph drainage of the area cannot be removed. It may, however, be the best one can do and it can be useful as a palliative measure for pain or impending fungation. This was the case in two of our patients:

1. A child of five, had an early recurrence after two courses of radio-therapy for a rhabdomyosarcoma of the orbit, and pain was very severe. The operation controlled the pain and fungation until shortly before his death 2 months later.

2. This patient had a blind painful eye, with increasing proptosis, and was found to have extensive retrobulbar extension from a malignant melanoma of the choroid. In spite of this she made a good recovery and the socket healed well. She is now, 2½ years later, suffering from intrathoracic secondaries, but has had no trouble or discomfort with the socket.

In three other cases, a malignant melanoma of conjunctiva, a small extra-ocular extension from malignant melanoma of choroid, and a mixed tumour of the lacrimal gland (associated with a blind and disfiguring eye), there is more hope that the operation may have been curative, though the follow-up is so far only short; 3½ years, 2¼ years, and 1 year respectively. The four surviving patients have all been fitted with satisfactory prostheses, and have been cheerful and unconcerned about their deformity.

This alginate mould has proved very satisfactory in use. These substances have obvious advantages over " Stent ", which is a difficult material to sterilize and handle, and which lacks elasticity; they also have the following advantages over the usual dental impression materials: they are supplied

sterile, and can be resterilized easily; no special temperatures, or measurements of quantities are needed; the mould does not shrink appreciably under the conditions described; breaks, cracks, and irregularities (*e.g.* those due to the tulle gras), can be repaired at once by using sodium alginate syrup and setting it with calcium chloride.

It is also easy to incorporate a handle into the mould, and to make a mould which completely fills the socket and covers its edges. When the skin graft is draped over it and the mould reinserted, the whole surface of the graft can be firmly pressed against its bed, thus ensuring the most favourable condition for taking.

Summary

An account is given of practical details in the operation for exenteration of the orbit. The advantages of using an alginate mould for applying the skin graft to the socket are stressed and the technique described in some detail.

The alginate materials described are marketed by Medical Alginates Ltd., Wadsworth Road, Perivale, Middlesex.

The prosthesis shown in Fig. 4 (*b*) was made by Mr. Brook at Queen Mary's Hospital, Roehampton, under the Ministry of Pensions.

The prosthesis shown in Fig. 5 (*b*) was made by Mr. Warren, of Clement Clarke Ltd., 16, Wigmore Street, W.1.

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OCULAR PALSIES FOLLOWING RETROBULBAR INJECTION OF ACETYL CHOLINE FOR RETINAL ARTERIAL OCCLUSION*

BY

IAN W. PAYNE and HOWARD REED

London

WE have been able to trace the records of 73 cases of retinal arterial occlusion seen at the Royal Eye Hospital, 22 of which were treated by injecting acetyl choline. The results are shown in the Table.

TABLE

VISUAL RESULTS OF INJECTION OF ACETYL CHOLINE IN 22 CASES

Case No.	Age	Delay in Treatment (hrs)	Dose (g.)	Route	Visual Acuity	
					Before	After
‡1	54	48	0.05	Retrobulbar	6/12	6/12
*2	64	60	0.05	Subconjunctival	Perception of light	6/60
3	38	48	0.1	Subcutaneous 2	No perception of light	No perception of light
4	47	Not known	0.1	Retrobulbar	? Perception of light	1/60
5	54	Not known	0.1	Retrobulbar	Counting fingers	Counting fingers
‡6	66	Not known	0.05	Retrobulbar	6/9	6/9
†7	70	Few	Moryl–0.00025	Subcutaneous 3	No perception of light	No perception of light
†8	32	Not known	0.05	Retrobulbar	3/60	3/60
9	53	Not known	0.05	Retrobulbar	Counting fingers	Counting fingers
*10	46	36	0.1	Retrobulbar	Counting fingers	Counting fingers
11	77	12	0.05	Retrobulbar	Perception of light	6/12
†12	42	24	Moryl–0.00025	Retrobulbar	Counting fingers	Counting fingers
†13	64	24	Moryl–0.00025	Retrobulbar	3/60	1/60
14	67	12	0.05	Retrobulbar	6/36	6/36
†15	63	24	0.05	Retrobulbar	No perception of light	No perception of light
‡16	62	72	0.05	Retrobulbar	6/9	6/9
17	67	1 week	0.05	Retrobulbar	Hand movements	Hand movements
18	66	96	0.05	Subconjunctival	Hand movements	Hand movements
19	75	36	0.05	Retrobulbar	6/60	6/24
†20	42	72	0.05	Retrobulbar	Perception of light	Perception of light
‡21	25	6	0.05	Retrobulbar	6/9	6/9
*22	33	1½	0.05	Retrobulbar	No perception of light	Perception of light

*Cases 2, 10, and 22 also had a paracentesis, and Case 2 retrobulbar procaine.
†Cases 7, 8, 12, 13, 15, and 20 were thought to be embolic.
‡Cases 1, 6, 16, and 21 showed branch occlusion.

*Received for publication June 26, 1953.

Results

In only one case of the total of 73 cases was any improvement in vision recorded. Unfortunately the majority of these cases were not seen until the occlusion had been present for several days. The reason for this delay in seeking treatment is partly due to the fact that many of these patients had experienced recurrent attacks of transient loss of vision due to retinal artery spasm with complete recovery of vision. When the final occlusion occurred they awaited the accustomed return of sight for hours or days, so that by the time advice was sought the spasm had become an organic occlusion.

All that treatment can be expected to do is to relieve spasm, so that it is only in those few cases which are seen very early that visual improvement is possible. Even if sight returns after treatment it is difficult to decide whether the relaxation of the spasm was assisted by treatment or would have occurred spontaneously. More careful studies on the results of the use of the various vasodilators in early cases are needed before the value of treatment can be properly assessed.

Case Reports

Five cases examined by the authors developed ocular palsies after the retrobulbar injection of acetyl choline.

Case 10.—Here there was an almost complete external ophthalmoplegia, only the superior oblique being intact, and in addition a small fixed pupil and corneal anaesthesia; 4 weeks later the pupil was dilated and fixed, and the other signs unchanged. The external muscles recovered after 3 months, but 3 years afterwards the cornea was still anaesthetic, and the pupil still fixed and dilated. The corneal epithelium was intact despite the lack of sensation.

Case 14.—This patient showed a palsy of the superior rectus, inferior oblique, and levator palpebrae, with fixed dilated pupil and absent corneal sensation; 2 months later the ocular movements were normal, but there was still a moderate ptosis, and a tarsorrhaphy was performed to protect the anaesthetic cornea; 8 months after the injection the pupil and extra-ocular muscles appeared normal, but the corneal sensitivity was still impaired.

Case 19.—This patient showed ptosis and defective elevation of the eye, with corneal anaesthesia and a fixed semi-dilated pupil; 6 months later the corneal anaesthesia and pupillary paresis were unchanged, but there was some recovery of the extra-ocular muscles.

Case 20.—This patient developed an inferior rectus palsy, but was not seen again until 14 months after the injection, when the palsy had recovered.

Case 22.—A complete external rectus palsy developed within 2 hours of the injection, but there was no pupillary anomaly or interference with corneal sensitivity. There was a somewhat questionable visual improvement after the injection, but a paracentesis performed some 4 hours later was followed by objective improvement in the circulation, the patient counting fingers in the lower field. The palsy is now—5 weeks after the injection—showing signs of recovery.

Aetiology of Ocular Palsy

Several cases of retinal arterial occlusion treated by the injection of acetyl choline are recorded in the literature, but we have been unable to find any reference to ocular palsy complicating its use.

In view of the very large numbers of retrobulbar anaesthetics which are administered in an eye hospital without this complication, we feel that these ocular palsies cannot be accounted for on the basis of mechanical trauma from the needle. It would therefore appear that they are due to the action of the acetyl choline itself, but the mechanism involved is obscure.

In no case was the fourth nerve involved, and it would appear that the acetyl choline injected into the muscle cone diffuses through this space, and may affect any of the nerves within it. It is interesting that the trigeminal nerve fibres supplying the cornea and the pupillomotor fibres seem to be damaged most severely. The loss of the consensual reflex in the affected eye indicates that the lesion is in the efferent pathway.

Pharmacology

Acetyl choline is the naturally occurring humoral transmitter at autonomic ganglia, parasympathetic nerve endings, and voluntary neuro-muscular junctions. It dilates arteries and arterioles, having its maximum effect in about half an hour, and it is for this reason that it is used in cases of arterial occlusion. Capillaries are not affected.

It also produces contraction of voluntary muscles by virtue of its physiological action on the motor end-plates of the nerves to these muscles. The extra-ocular muscles are unusually sensitive to its action. It has been shown experimentally that massive doses of acetyl choline may depolarize the muscle end-plate, thus causing temporary paralysis of the muscle, a blocking action which would be reinforced by the acetyl choline which is normally liberated at the nerve ending in constant but small amounts.

Acetyl choline is normally rapidly destroyed by cholinesterase in the tissues, and it is therefore difficult to explain the long duration of the palsies described. Further, the anomalous behaviour of the pupil in Case 10 and the anaesthesia of the cornea in three other cases remain unexplained.

Summary

Five cases are described in which ocular palsies followed the retrobulbar injection of acetyl choline. In each case the extra-ocular muscles were affected, and in three a pupillary palsy and anaesthesia of the cornea were also produced. The extra-ocular palsies show a tendency to slow recovery, but there has been no improvement in the corneal sensation, or pupillary reflexes.

We wish to thank the surgeons of the Royal Eye Hospital for allowing us access to their cases, and Professor Arnold Sorsby for his helpful criticism in the preparation of this paper.

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APPLIANCES

ANGLE OF THE ANTERIOR CHAMBER VIEWED BY TRANSMITTED LIGHT*

BY

J. H. DOBREE and E. F. FINCHAM

From the Institute of Ophthalmology, London

THE viewing of translucent structures by transmitted light is a well established practice in ophthalmology, but so far does not seem to have been applied to the region of the angle of the anterior chamber. A simple and effective method of transillumination has been devised, and, as certain structures in this important region show to better advantage under these conditions, the technique is presented and some preliminary observations on about 100 eyes recorded.

METHOD

A minute endoscopy lamp (2.5.-v. cystoscope lamp made by Rimmer) lies in a perspex lamp holder which has a narrow hole bored along its entire length (Fig. 1). The bulb almost touches the rim of a Goldmann gonioscope, and the small air-space surrounding it prevents excessive heating. The base of the lamp is connec-

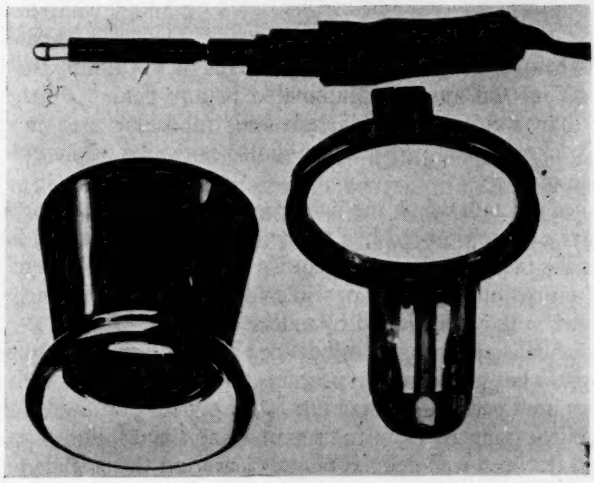

FIG. 1.—Component parts.

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ted to a 3-v. battery by two fine wires. The apparatus is fixed on to the gonioscope by a metal collar with the lamp opposite the viewing mirror (Fig. 2).

FIG. 2.—Apparatus assembled.

In most instances, the gonioscope, with the transilluminating system attached, was used in conjunction with a modern Zeiss slit-lamp so that any particular field could be illuminated, either by transmitted light using the new attachment or by reflected light through the orthodox illuminating system of the slit-lamp, and, by simply switching from one system to the other, a direct comparison of the two methods of illumination could be made.

APPEARANCE OF THE NORMAL ANGLE SEEN BY TRANSMITTED LIGHT

The intensity of illumination obtained by the system described is unexpectedly brilliant, being approximately equal to that obtained with a 3-mm. wide slit-lamp beam. The bulb throws a diffuse patch of light over several square millimetres of the limbus so that an arc of about 60° of the angle is illuminated in any field. Furthermore, this spread of light was found to include the trabecular area in eyes having abnormally large or small corneae, so that the position of the bulb is effective for any size of eye.

The tissues through which the light passes contain many blood vessels and these impart a somewhat red hue to the picture. A more striking difference however is the fact that the cornea and sclera are rendered more transparent by transillumination, and it is possible to see further into their depth than is the case when they are viewed by reflected light.

The trabecula is particularly well defined and shows up as a honey-coloured band of somewhat gelatinous appearance in sharp contrast with the cornea, which takes on a pearly-white colour. Any pigment on the trabecula stands out in excellent contrast from the surrounding tissues, and pigment patches often stand out in a well-defined plane, clearly on the surface rather than in the substance of the tissue.

The vessels in the vicinity of the angle, which are almost invisible by the usual method of illumination, are shown up to advantage by trans-

illumination. Blood filling the canal of Schlemm is easy to identify and corneal capillaries can often be seen in the depths of the tissue extending beyond Schwalbes line towards the centre of the cornea. Larger vessels lying near the limbus, such as forwardly placed anterior ciliary arteries, can sometimes be plainly seen, looping deeply to disappear behind the trabecula in the depths of the angle. Observation of these vessels is further facilitated by the incorporation of a yellow/green filter in the viewing system.

Some Appearances seen in Pathological Angles viewed by Transmitted Light

(*a*) *Iris Inclusions.*—Iris tissue lying in the substance of the cornea and sclera is usually invisible when viewed by the orthodox method. When seen by transmitted light, however, iris inclusions, whether caused by operation or trauma, are much more readily visible and their size and extent can often be made out. It is thought that extensions into the fibrous tunic from malignant melanomata of the iris or ciliary body will be found to show up in much the same way.

(*b*) *Narrow Angles.*—The apex of a narrow angle, which usually appears as a dark cleft when viewed by the orthodox method, is easier to see when illuminated through the cornea. The position of the anterior edge of the trabecula and the presence of synechiae within a narrow angle are often easier to identify by this method.

(*c*) *Peripheral Anterior Synechiae.*—Transillumination often shows these structures to be of a very much looser and more spongy texture than they appear when seen by reflected light. Some of the less pigmented types are, however, less clearly seen by transillumination, since, being rendered more translucent, they are not so well defined as when they are seen by reflected light.

Comment

The main disadvantages inherent in illuminating the angle by a bulb attached to the gonioscope are that a certain amount of heat is generated and that the leads are an additional encumbrance. Patients often experience a sensation of warmth and it is our practice to switch off the current for 10 seconds in every minute to allow the heat to disperse, but as no thermal reaction in the conjunctiva has been encountered even this may be an unnecessary precaution.

Although the leads are found to be a disadvantage when they are used in conjunction with a slit-lamp, it must be pointed out that the observer is entirely independent of any rigid system of illumination (or for that matter of a fixed magnifying system) and neither slit-lamp beam not deviating prism is required. Furthermore, the attachment can be used with the patient in any position and it could easily be adapted to devices in use for goniotomy.

We are indebted to Messrs. N. Roberts and F. H. Sheen for constructing the apparatus and to the Department of Medical Illustration, Institute of Ophthalmology, for the photographs.

Brit. J. Ophthal. (1954) **38**, 52.

FLUOROPHOTOMETRIC APPARATUS FOR THE OBJECTIVE DETERMINATION OF FLUORESCENCE IN THE ANTERIOR CHAMBER OF THE LIVING EYE*

BY

MAURICE LANGHAM AND KENNETH C. WYBAR

From the Institute of Ophthalmology, London

FOR many years considerable attention has been focused on the problem of the origin and circulation of the aqueous humour under normal and pathological conditions. One of the methods applied to this study is the detection within the eye of dyes which enter the anterior chamber across the blood-aqueous barrier—a method first suggested by Ehrlich (1882) when he observed that fluorescein injected intravenously passes into the aqueous humour. Ehrlich anticipated that the use of this dye would promote a deeper understanding of the problem, and many ways have since been devised of determining the presence of fluorescein in the eye of the living animal. In the present paper an instrument is described which permits an objective determination of the degree of fluorescence under experimental and clinical conditions.

Apparatus

The main component parts and optical principles of the fluorophotometer are illustrated in Figs 1 (*a*) and 1 (*b*). Light from the anterior chamber passes through a 1-inch objective lens, and is transmitted partly through the monocular microscope tube and eyepiece to the observer, and partly, after reflection, to the cathode area of a photo-electric multiplier tube (RCA 931A). The reflector lying immediately behind the objective lens comprises a completely silvered mirror mounted on a pivot arm in such a way that the angle between it and the incident light can be adjusted to ensure reflection of the light from the anterior chamber to the centre of the cathode area of the photo-electric multiplier tube; this is determined by replacing the case containing the tube by a holder with a ground glass screen on which the reflected light can be viewed. Once the mirror has been set at the correct angle it may be fixed by means of a small locking screw. The size of the image falling on the photosensitive area of the photo-electric multiplier tube may be limited by the introduction at the focal plane of a diaphragm varying in size and shape with the area of the anterior chamber to be studied. Without the introduction of a diaphragm the effective area of the field of view is 15 mm. in diameter, equivalent to an actual field of view of 4·54 mm., the objective lens giving a linear magnification of 2·75. In practice, however, a diaphragm 1–2 mm. in diameter is used to limit the field to a narrow area of the anterior chamber, which in the rabbit is approximately 3 mm. in depth.

The photo-electric multiplier tube is a high vacuum photocell with a maximal response at 4000 Å. The photo-electric current produced at the cathode is multiplied many times by secondary emission occurring at successive cathodes within the valve. The tube used in the apparatus is supplied by a series of H.T. dry batteries, the voltage of which is equally distributed by means of a group of nine micro-resistances incorporated

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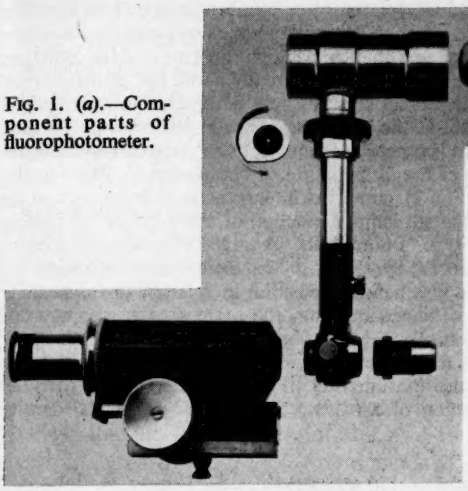

FIG. 1. (*a*).—Component parts of fluorophotometer.

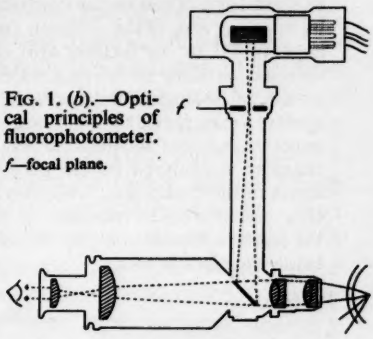

FIG. 1. (*b*).—Optical principles of fluorophotometer.
f—focal plane.

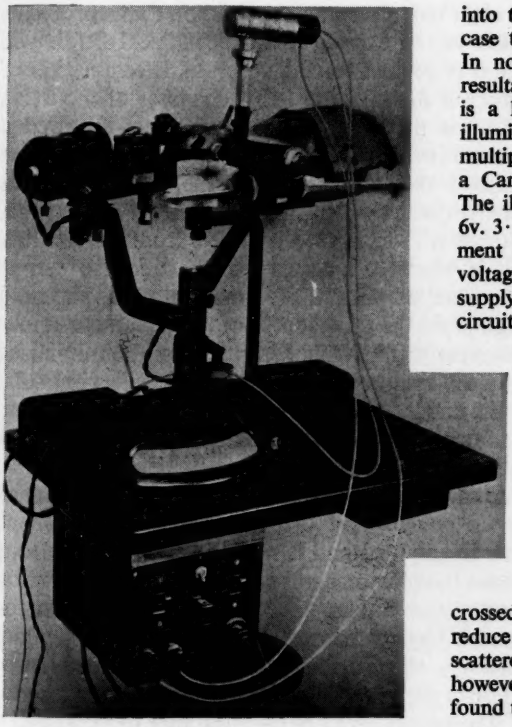

FIG. 2.—Fluorophotometer mounted on Haag-Streit slit lamp.

into the base of the photomultiplier case to the nine secondary cathodes. In normal operating conditions the resultant output current from this tube is a linear function of the exciting illumination. The output of the photomultiplier tube is recorded directly on a Cambridge damped galvanometer. The illumination system comprises a 6v. 3·5 amp. bulb with a vertical filament energized through a constant voltage transformer from the mains supply. Where necessary a second circuit is introduced to provide increased illumination by supplying the bulb with a further 2 volts.

There are two refinements which may be incorporated into the instrument. First, a colour filter (Ilford 605 or 625) may be placed in front of the cathode area to allow preferential transmission of fluorescent light; secondly, crossed polaroids may be fitted to reduce the effect of reflected and scattered light. In animal studies, however, these modifications are not found to be necessary.

The fluorophotometer is mounted on a conventional Haag-Streit slit

lamp wherein the binocular microscope is replaced by a monocular one (Fig. 2). The observer views the anterior chamber through the microscope, and adjusts the angle between the arm carrying the microscope and that carrying the light to give the optimum view of the anterior chamber. This angle, which is normally about 60°, is maintained throughout the experiment. The focal vertical beam of light is adjusted to the required intensity by varying the width of the slit at the beginning of the experiment, and is then left unaltered. The stability of this light is generally adequate, but a photocell is employed to maintain a check on the constancy of the illumination. The photocell, fitted to the illuminating arm of the slit lamp (*see* Fig. 2), comprises a plane glass slide inclined at an angle of 45° to the incident arm of the slit lamp, a fraction of the incident light being reflected vertically to fall on a barrier type of photocell. A target, consisting of a series of concentric rings, is incorporated into the eye-piece, so that before each recording the observer may check that the rings are in a constant position in relation to the cornea-aqueous and lens-aqueous barriers. This ensures that the same area of the anterior chamber is analyzed by the photomultiplier tube during each recording. In the later stages of the experiment, when there is a high concentration of fluorescein in the anterior chamber, it may be necessary to reduce the intensity of the fluorescent light reaching the photomultiplier tube by the insertion of a neutral filter of known optical density below the cathode area.

Discussion and Results

It is becoming increasingly clear that a satisfactory solution to the problems of intra-ocular dynamics, both in the experimental and clinical fields, will not be achieved until a method is devised for the accurate determination of the concentration of substances in the intact anterior chamber of the living animal. Up to the present time these dynamic studies have followed a similar pattern. The concentration of a substance in the plasma is raised and its time-course compared with the concentration in the aqueous humour removed from each eye at predetermined times. The limitations of this method, only too well recognized by those who have used it, follow from the fact that withdrawal of aqueous humour leads to a marked increase in the permeability of the blood-aqueous barrier with the formation of a plasmoid aqueous, so that only two points on the time-course of the aqueous humour can be obtained for any one experiment. This drawback can be minimized to a certain extent by pooling the results obtained from numerous animals; the work of Palm (1947) on the entry of radioactive phosphate, and of Maurice (1951) on the entry of radioactive sodium are excellent examples of what may be achieved, although the inherent variation between different animals, even between members of the same species, limits the interpretation of such a composite study.

A modification of this experimental method is seen in the work of Bárány and Kinsey (1949), who utilized the phenomenon of the rapid renal excretion of certain compounds to study the rate of their disappearance from the aqueous humour. For example, by raising the concentration of *p*-amino-hippuric acid in the plasma for a sufficient length of time, a stage may be reached when the concentration of the tracer substances in the aqueous humour exceeds that in the plasma. The rate of decay of the substance in the aqueous

humour is then determined by examining the aqueous removed from the other eye after a certain interval. The results obtained by this method are susceptible to mathematical analysis and important conclusions on the rate of flow of aqueous humour have been drawn.

In considering the problem of diffusion in the eye, it is known that a substance may pass into the anterior and posterior chambers from the uveal tract across the blood-aqueous barrier, but it is not justifiable to assume that in the early stages the substance exists in the two chambers in equal concentrations, although, in the presence of the circulation and flow of aqueous humour, the substance may eventually become evenly distributed throughout its volume. The substance will continue to accumulate in the aqueous humour until a state of dynamic equilibrium* is reached between its concentration in the plasma and in the aqueous humour, the so-called *steady state*, at which point the rate of accumulation is zero. After the steady state has been attained, the rate of replacement of the substance from the blood falls below its rate of disappearance from the aqueous, and its concentration in the aqueous humour is lowered until it is completely eliminated. During this diminishing phase the substance may once more become unevenly distributed throughout the aqueous humour.

Several methods have been described previously for assessing the concentration of fluorescent dyes in the aqueous humour of the living eye after intravenous injection. Amsler and Huber (1946) examined the anterior chamber at frequent intervals through the corneal microscope after the intravenous injection of fluorescein, the focal beam from the slit lamp directed into the eye being reduced in intensity by means of a resistance in the lamp circuit until the fluorescence of the aqueous was just imperceptible. This is regarded as a measure of the concentration of fluorescein in the aqueous at that particular time, the degree of fluorescence of a solution within the concentrations studied, being taken as inversely proportional to the quantity of light required to make it just perceptible, although the relationship is not linear. Goldmann (1949), on the other hand, assessed the concentration of fluorescein in the aqueous at frequent intervals by adjusting a standard fluorescent beam so that it matched the fluorescence of the aqueous observed simultaneously through a corneal microscope.

The instrument described above has been designed to record objectively the relative changes in concentration of a fluorescent substance in the anterior chamber of the eye, and is of value not only in detecting gross differences in the permeability of the blood-aqueous barrier clinically, but also in studying the wider problems of the flow of aqueous humour experimentally; it is of particular value in animal studies when high concentrations of the dye may be used. The interpretation of the results is based on the observation that the intensity of fluorescence, and in consequence the output

*The state of dynamic equilibrium differs from that of chemical equilibrium in that a balance is reached between a substance on either side of a living membrane without necessarily inducing the same concentration of that substance in each chamber.

of the photo-electric multiplier tube, is directly proportional to the concentration of fluorescein. This relationship was determined by measuring with the fluorophotometer the fluorescence of various solutions containing a known concentration of fluorescein. These solutions, placed in a square-shaped cell of fused silica glass were illuminated by the focal light from the slit lamp, and observed with the fluorophotometer through one of the cell faces lying parallel with the light beam. It will be noted that over a wide range of concentration of fluorescein the relationship is strictly linear (Fig. 3).

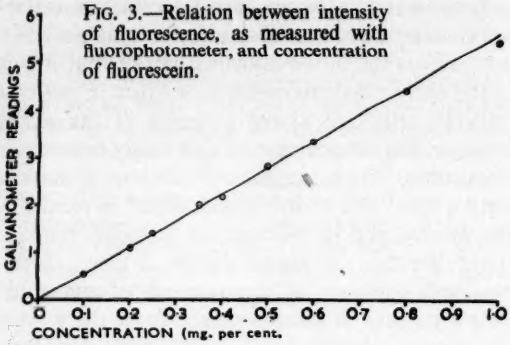

FIG. 3.—Relation between intensity of fluorescence, as measured with fluorophotometer, and concentration of fluorescein.

An attempt has been made with this apparatus to overcome certain of the difficulties encountered in an approach to this problem. First, by limiting the effective field of view to a constant area of the anterior chamber throughout the period of the experiment, any inconsistencies due to an uneven concentration of the dye in the aqueous are largely eliminated. Secondly, by being able to record the concentration of the fluorescein within the aqueous at frequent intervals without disturbing the integrity of the blood-aqueous barrier, the changes in the concentration of the dye are obtained over the complete time-course. These results may then be correlated with the time-course of the dye in the plasma, and from this the constants of penetration and exit, and the rate of flow of aqueous humour may be calculated.

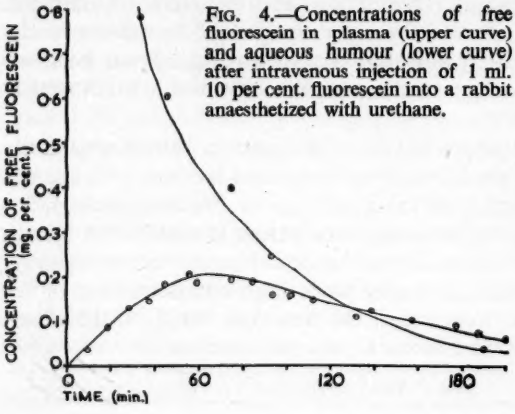

FIG. 4.—Concentrations of free fluorescein in plasma (upper curve) and aqueous humour (lower curve) after intravenous injection of 1 ml. 10 per cent. fluorescein into a rabbit anaesthetized with urethane.

There are, however, certain disadvantages in this approach. First, there are not many compounds which are suitable for such a study, fluorescein and eosein being two of the few dyes which may be used in appropriate concentrations. Secondly, since a high proportion of these dyes become bound to the plasma proteins, to which the normal blood-aqueous barrier is almost

impermeable, only that fraction of the dye which is not bound or adsorbed in this way diffuses into the aqueous humour. Furthermore, it is possible that some of the free dye in the aqueous may also be lost by becoming bound to the proteins of the tissues lining the anterior chamber.

An example of the type of results which may be obtained in the rabbit after intravenous injection of 1 ml. of a 10 per cent. solution of fluorescein is shown in Fig. 4. The rabbit is maintained in position throughout the period of the experiment in a specially designed cradle attached to the table of the slit lamp (*see* Fig. 2). Samples of blood are taken at periodic intervals, and analysed for total and freely diffusible fluorescein. The degree of fluorescence in the aqueous humour is measured by the fluorophotometer. At the end of the experiment the aqueous is removed and analysed for fluorescein, and by correlating this analysis with the final fluorophotometric reading it is possible to translate the other readings into absolute values.

Summary

(1) A description is given of a simple apparatus which fits on to a conventional Haag-Streit slit lamp and enables objective measurements to be made of the degree of fluorescence in the anterior chamber of the living eye.

(2) There is a linear relationship between the concentration of fluorescein in a solution and the degree of fluorescence of the solution as measured by the fluorophotometer over a wide range of concentrations of fluorescein.

(3) The application of this technique to dynamic studies of the formation and outflow of the aqueous humour in animals and man is considered.

We should like to thank Sir Stewart Duke-Elder for his help and interest during the course of this work, and the Medical Research Council for defraying the cost of the research. We are also indebted to Messrs. N. Roberts and A. Church for the assembly of the fluorophotometer.

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Brit. J. Ophthal. (1954) 38, 58.

CASE NOTES

A CASE OF MENINGITIS APPARENTLY SECONDARY TO HERPETIC KERATITIS AND POSSIBLY PRECIPITATED BY CORTISONE TREATMENT*

BY

CHRISTOPHER HEATH

Redruth, Cornwall

As the effect of cortisone in lowering resistance to infection is now recognized, and as it has been suspected for some time that meningeal involvement sometimes occurs with virus infections of the eye, this case, although unproven, seems of sufficient interest to be worth recording.

Case Report

A man aged 43 first attended the eye clinic on July 18, 1952.

History.—He stated that he had had several severe attacks of dendritic ulceration of the right eye whilst in the Navy, starting in 1932. He was thrice invalided home from abroad, and was finally, in 1947, invalided out of the service for this cause. Until the present attack, however, he had had no recurrence since an attack after a bout of malaria in 1945. Visual acuity in the right eye on discharge from the Navy was 6/18. He had had herpes on his face in childhood and occasionally up to the time of his first dendritic ulcer in 1932; this attack occurred when he was 2 weeks convalescent from measles and facial herpes developed 2 weeks later. He was doubtful whether he had ever had herpes again since that time. He had been vaccinated more than six times during his 23 years' service. He had had several bouts of malaria, but only in 1945 in Africa was this associated with corneal ulceration; he had had no malaria since 1947.

Examination.—His right eye had been sore and under treatment for 2 weeks before he attended the clinic. He had been in good health and had neither a cold nor herpes nor any apparent malady to precipitate the attack. His last illness had been bronchitis 7 months before. Vision in the right eye was reduced to 6/60 by active general superficial keratitis; this was largely of punctate type with a suggestion of dendritic ulceration in one area, but the appearance was obscured by treatment and by the gross underlying scarring. There was secondary iritis. The left eye was normal.

Therapy.—As it was thought that the cornea was already too severely damaged to tolerate painting with iodine, treatment was started with atropine and aureomycin ointment and a week later the condition appeared much improved. After another fortnight the cornea was healing so well that the patient was advised to continue with the atropine for another 4 weeks and then to desist if all seemed well.

Further Developments.—On September 2, 1952, however, he returned to the clinic because the eye had become painful again; 10 days later its appearance suggested the onset of atropine irritation and bullae of the corneal epithelium began to form. Under treatment with lachesine drops and emollient applications the eye became more painful and the patient was admitted to hospital on September 25.

There was now a general keratitis with secondary iritis and spastic pupil; corneal sensation was not appreciably impaired. The patient was in good general health.

*Received for publication July 17, 1953.

Further Therapy.—As the eye now appeared irritable to treatment, gutt. cortisone acetate 0.5 per cent. twice daily was prescribed to combat this, with gutt. hyoscin 0.5 per cent. twice daily and heat; with this the eye improved steadily.

Development of Meningitis.—On October 7, 12 days after admission, the patient complained of severe frontal headache. This was not accompanied by any apparent change in general condition, temperature, or pulse; the eye condition remained the same and no other physical signs were elicited. Throughout the next and most of the following day the headache persisted, but the situation seemed otherwise unchanged. On the evening of October 9, the third day of the headache, the patient's temperature rose to 103° and he noted some deterioration of vision of the right eye, which had, however, been only " hand movements " previously. Examination at that time showed slight loss of upward movement of the eye and some stiffness of the neck; reflexes were normal and no other physical signs elicited. Next morning, for the first time, the patient appeared seriously ill; his temperature was 102°; his right eye had lost all movement, and had no perception of light, and the tension was low; the fundus could not be seen; the left eye was normal. The assistance of the Ear, Nose, and Throat department was sought, to exclude the possibility of sinus involvement, and also of the physicians, who confirmed the diagnosis of meningitis, performed a lumbar puncture, and instituted intrathecal penicillin therapy.

Next morning there was little change in the general condition; the pyrexia remained unabated; a prolific crop of herpes simplex appeared on the patient's face, mainly on the right side. Lumbar puncture and treatment was repeated.

The report on the cerebrospinal fluid of the previous day showed a slightly turbid fluid with no clot formation, 450 cells per cmm. (polymorphs 70 per cent., lymphocytes 30 per cent), protein 190 m. per cent., globulin (N.A.) increased, chlorides 700 mg. per cent., sugar 80 mg. per cent.; no growth was obtained on culture.

In the afternoon examination showed impairment of inward, upward, and downward movement of the good left eye and apparent contraction of the peripheral field of vision. The fundus was normal. The alarming inference that the left eye was about to follow the example of the right, coupled with the normal sugar content of the cerebrospinal fluid and the failure to isolate any organism, enhanced an earlier suspicion that the progress of the malady might be due to direct spread of the herpes virus from the affected eye; treatment with aureomycin was therefore started at once. Next day the patient felt better, his temperature fell to 100.2° and the field of vision appeared full.

Recovery.—On the following day (October 13) his condition was much improved, and his temperature normal. The right eye had bare perception of light, but was otherwise unchanged; the left eye had a partial oculo-motor palsy and good vision.

From the second day of treatment with aureomycin the patient made a steady recovery; by the third day movement of the left eye was improving and on the fourth day it appeared full. By October 21 the right eye also had recovered fair movement; vision seemed still reduced, but this was difficult to assess because of the keratitis. By October 28, vision had improved to " hand movements " again, and local treatment was continued with lachesine and hyoscine. A rather atypical deep, disciform keratitis subsequently developed. The patient recovered his general health and was discharged from hospital on November 5.

He continued to attend the clinic, and the right eye improved steadily. All movements except full abduction were restored by December 9, and this also returned a month later; vision is still limited to hand movements, but it is not possible to assess whether this is due only to the gross corneal scarring and adherent pupil or to neural damage. The left eye is normal.

Pathological Investigation.—Samples of the cerebrospinal fluid and blood were submitted to the Virus Reference Laboratory, Public Health Department, Colindale, Middlesex; no organism was discovered; leptospiral agglutination and complement-

fixation tests for lymphocytic choriomeningitis were negative. In later specimens of cerebrospinal fluid more than 80 per cent. of the white cells were lymphocytes.

It seems most likely that this dramatic illness was a virus meningitis, presumably that of herpes simplex. If this be granted, it remains to enquire why this does not appear previously to have followed the common herpetic infections of the eye. It is suggested that the solution of this problem is to be found in the effect of cortisone treatment in reducing the local resistance to infection.

It is a pleasure to thank Dr. C. T. Andrews and Mr, M. R. Sheridan for their help in this and other cases.

Brit. J. Ophthal. (1954), 38, 61.

CASE NOTES

THREE THERAPEUTIC LAMELLAR GRAFTS*

BY

H. E. HOBBS

London

INDICATIONS for lamellar corneal grafts are somewhat more numerous than those for penetrating keratoplasty, and Paufique, Sourdille, and Offret (1948) mention, besides the usual optical reason for replacing a corneal scar, tectonic, preparatory, aesthetic, and therapeutic indications. This last, designed to interrupt the course of chronic and recurrent corneal disorders, is of peculiar interest, because, although it possibly provides the widest field of application of lamellar grafts, its rationale is less well understood. It is possibly for this reason that its employment depends even more on its proven successes than does keratoplasty performed on other indications. The idea of utilizing the trophic effects of a graft in this way is attributed to Filatov, in whose theory of " biogenic stimulants " it played but a small part, and it is perhaps because the success of other applications of this theory (*e.g.*, the use of subconjunctival injections of cod liver oil or implantations of placenta in the treatment of various forms of ocular disease) has not been as great as one had been led to expect that the therapeutic functions of the corneal graft have received less attention than might have been expected.

On the continent of Europe the therapeutic value of lamellar grafts was first demonstrated in France, notably by Paufique (1947, 1948), and Paufique and Bonnet (1948), and the largest series of reported cases (41) comes from his clinic (Hugonnier-Clayette, 1949). In Great Britain cases have been reported by Black (1949), Foster (1950), and Rycroft and Romanes (1952), and this effect of grafting was treated in some detail by Lister (1951) in his review of keratoplasty. The purpose of this paper is to add three more illustrative cases to those mentioned.

Case Reports

(1) A man aged 58 was first referred to me in December, 1950, because for rather more than a year he had had an irritable eye resistant to all forms of treatment elsewhere. Some 43 years previously bilateral congenital cataracts had been needled by Mr. J. H. Fisher at St. Thomas's Hospital, and after this the patient had enjoyed excellent vision until July, 1949, when he began to experience periodic irritation of the left eye with clouding of vision.

Examination.—Extensive corneal epithelial oedema of the left eye obscured any view of the fundus, but through it heterochromia of the iris could be seen. The possibility of this being due to glaucoma, either of the aphakic type, or resulting from late uveitis, was discarded in view of the absence of ocular hypertension or of inflammatory signs, and I accepted the condition as primarily corneal, a form of post-extraction corneal dystrophy.

* Paper delivered with demonstration of cases at the Royal Society of Medicine (Section of Ophthalmology on June 11, 1953.

Therapy.—Since the usual medicaments had had no effect, I treated the eye with cortisone by sub-conjunctival injection and drops. At first there did appear to be some effect in that there were periods of diminished epithelial oedema and clearer vision, which tended to occur early in the day, and in February, 1951, when he came to my morning out-patients session, his corrected visual acuity, which had presented as finger-counting 2 months earlier, was 6/12. This improvement, however, did not last, and 6 months later cortisone was producing no effect. As time went on the irritative symptoms began to increase and early in 1952 he discussed with me the alternatives of retiring early on a disability pension, or having the eye removed.

Operation.—It seemed to me then that, although therapeutic grafts in oedematous corneal conditions are not universally successful (Hugonnier-Clayette, 1949), a graft ought to be given a trial in these circumstances. On March 29, 1952, therefore, I performed a 7-mm. lamellar graft.

Result.—His convalescence was uneventful so that within 3 weeks the eye was quiet, and since then it has remained so in spite of the fact that some epithelial oedema has reappeared during the last 6 months. Visual improvement was not primarily sought here and none has been obtained, and the prognosis must still be considered doubtful in view of the recurrent epithelial oedema; but I feel that, in the circumstances, keratoplasty has been justified, and I should not hesitate to repeat the operation if the irritation recurs.

(2) **A man aged 62** was referred to me by Mr. Frederick Ridley in December, 1951, with an irritable eye resulting from a disciform keratitis of some 2 months' duration.

Therapy.—He showed some subjective improvement under local treatment with cortisone during the first 6 weeks; but it became apparent as the cornea cleared that there was an accompanying uveitis with firm posterior synechiae which tethered the pupil, and although treatment was continued over the next 9 months the eye still tended to be irritable unless drops were continuously used.

Operation.—In December, 1952, therefore, the question of a therapeutic lamellar graft was considered and on January 21, 1953, I performed a 7-mm. lamellar keratoplasty.

Result.—Convalescence from this was uneventful, and although deep corneal vessels rapidly reformed in the graft bed the graft itself remained clear in spite of the presence of some epithelial oedema, and the eye was quiet without treatment. Vision was not improved because of the lens opacity. The eye has so far remained quiet during the succeeding 5 months, although the vascularity and some epithelial oedema remain.

(3) **A man aged 42** was referred to me for cortisone treatment by Mr. Eugene Wolff just 2 years ago with a history of deep keratitis of doubtful origin of 20 years' duration. Little useful vision had been present in the eye since the original attack, and it was subject to recurrent attacks of irritation in which the dense corneal nebula became vascularized. In May, 1951, the eye was suffering one of these relapses and exhibited a vascularized, densely opaque cornea.

Therapy.—Cortisone administered locally rapidly produced a quiet eye; but, somewhat to my surprise, the long-standing nebula began to clear and a month later the iris could be seen above. Continued treatment resulted in further clearing and slight visual improvement to finger counting; but this was the limit of his progress, and although the eye remained quiet on cortisone, one effect of which appeared to be to enable him to tolerate mydriatics, irritation recurred when it was withdrawn. The appearance of the eye in a quiet phase in August, 1951, is shown in Fig. 1 (opposite).

Operation.—In May, 1952, therefore, Mr. Wolff and I discussed the advisability of a therapeutic lamellar graft and this was performed, by him, on September 5.

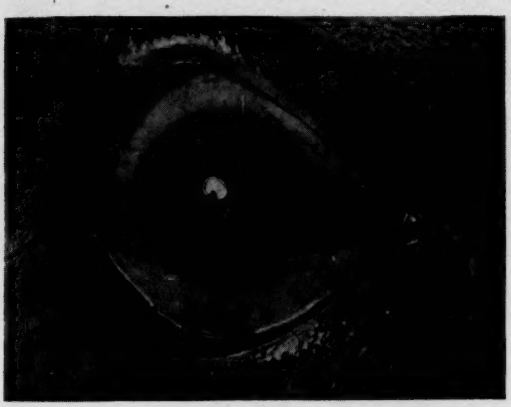

FIG. 1.—Case 3, appearance in August, 1951.

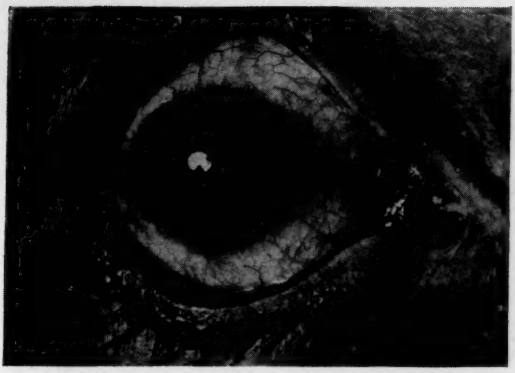

FIG. 2.—Case 3, appearance in June, 1953.

Result.—Convalescence was uneventful, and since this time increased clearing of the surrounding cornea has been seen, so that the condition, as it appeared in June, 1953 (Fig. 2), contrasts quite favourably with the original state. Here again, visual improvement was not a primary indication for the operation, but some degree of improvmeent has been obtained and he has recently been able to distinguish 6/60.

I am indebted especially to Professor L. Paufique for his kindness and instruction during the period I spent in his clinics, and I should like to thank Mr. Eugene Wolff and Mr. Frederick Ridley for their permission to include their cases in this report. The photographs of the last case were made by the Department of Medical Illustration, Institute of Ophthalmology, London.

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NOTES

MIDLAND OPHTHALMOLOGICAL SOCIETY

Programme of Meetings, 1954.

March 16, 1954, at 3 p.m., at the Northampton and Kettering General Hospital, Billing Road, Northampton.

April 30, 1954, at 3 p.m., at the Wolverhampton and Midland Counties Eye Infirmary, Compton Road, Wolverhampton. (Joint meeting with the North of England Ophthalmological Society).

June 26, 1954, at 10 a.m., at the Portsmouth and Southern Counties Eye and Ear Hospital, Pembroke Road, Portsmouth (Joint meeting with the Southern Ophthalmological Society).

September 24, 1954, at 2 p.m. Annual General Meeting at the Birmingham and Midland Eye Hospital (including the Middlemore Lecture).

November 23, 1954, at 3 p.m., at the Derbyshire Royal Infirmary, London Road, Derby.

Honours

Sir Stewart Duke-Elder received a Doctorate in the Faculty of Medicine *honoris causa* of the University of Strasbourg, together with the University Medal, on November 23, 1953.

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